

**SAJOUS'S**  
**ANALYTIC CYCLOPEDIA**  
**OF**  
**PRACTICAL MEDICINE**

**BY**  
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**WITH THE ACTIVE CO-OPERATION OF OVER**  
**ONE HUNDRED ASSOCIATE EDITORS**

**TENTH REVISED EDITION**

**Illustrated with Full-page Half-tone and Color Plates**  
**and Appropriate Cuts in the Text**

**VOLUME FOUR**



**PHILADELPHIA**  
**F. A. DAVIS COMPANY, PUBLISHERS**  
**1922**





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# SAJOUS'S

## ANALYTIC CYCLOPEDIA

### of PRACTICAL MEDICINE

#### D

#### DIABETES INSIPIDUS (POLYURIA).—DEFINITION.—

Diabetes insipidus is a syndrome comprising several altogether dissimilar states, and characterized by marked increase in the quantity of urine, without any necessary qualitative changes in the elements of which it is composed.

**ETIOLOGY.**—While diabetes mellitus occurs most frequently in middle age, polyuria is not rare in childhood. One-half the cases start before the age of 35. In some families several polyurics may be found.

[In a case observed by Lauritzen, in a girl, 16 years old, four generations and 8 out of 19 members of the family had suffered from polyuria, viz.: the great-grandmother, 3 of her children, 3 grandchildren, and the great-grandchild,—the patient. The disease was, in all cases, directly inherited by the child from its parent, all the first-born being attacked. The great-grandfather suffered from enuresis, but not from polyuria. R. LÉPINE.]

Weil has reported the history of 4 generations of a family, including altogether 91 individuals, among which 23 suffered from diabetes insipidus.

In exceptional instances diabetes mellitus may be traced in the antecedents; much more frequently a

neuropathic tendency is found. Predisposition is a most important factor in the etiology of this affection.

As for the determining or accidental causes, in a certain number of cases the polyuria is referable to a traumatic factor, *c.g.*, a fall upon the head. Sometimes diabetes mellitus immediately follows the traumatism and it is only after a time, two months or more, that a change to diabetes insipidus occurs. There is, consequently, an undoubted connection between the two affections. This has likewise been shown by experimentation. Claude Bernard, in puncturing a certain spot in the floor of the fourth ventricle in a rabbit, caused diabetes mellitus, while in puncturing at a slightly different point he caused simple polyuria. There is, however, always some degree of uncertainty in this result, and it is by no means true that experimenters can *at will* produce polyuria by puncture of the floor of the fourth ventricle.

After traumatism of the cranium, the chronic lesions of the encephalon, and tumors in particular, occupy an important place in the etiology of polyuria. I have seen several cases of this kind. In one of them there

was found at the autopsy a tumor of the optic thalamus. The polyuria appeared very suddenly. The large size of the growth suggested that it might have compressed the pedicle of the pituitary.

Emotions and accidental causes also bear a relation to this affection.

Finally, the abuse of alcoholic beverages is a frequent cause of diabetes insipidus.

In children, one-tenth of the cases of diabetes insipidus have been observed to be preceded by some infectious disease.

The following will give an idea of the relative frequency of the different causes operating to produce diabetes insipidus:—

Heredity .....	10
Neuropathic disposition .....	20
Trauma of the skull, organic lesions of the encephalon (including syphilitic lesions) ....	30
Excesses of all kinds .....	15
Various accidental causes, including infectious diseases ..	25
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**PATHOGENESIS.**—Eckhard has, of all physiologists, been the most energetic in his advocacy of the hypothesis that there exist nerves which produce polyuria. In his experiments, indeed, he witnessed the occurrence of the latter after superficial excitation of the vermis, without any accompanying change in the aortic blood-pressure. Moreover, section of the splanchnic nerve is followed both by polyuria and lowered vascular tension.

As for the details of the mechanism through which there occurs in the kidney an increase of the excretion of urine, in cases where there is no primary dyscrasia and, in particular, no

excess of water in the blood-stream, they are still shrouded in obscurity. The circulation through the glomeruli is known to be increased, and the possibility that this occurs owing to relaxation of the arterioles must be admitted. A relaxation of the *efferent* vessel may, in particular, be supposed to occur. If this be the case, the blood-pressure must increase in the capillary network which follows the glomerulus, and the mechanical conditions for the reabsorption of water are unfavorable to its occurrence. The benefit conferred by vasoconstricting remedies (see Treatment) tends to support the idea that vasomotor relaxation is an important factor in the production of polyuria.

In a few cases,—on the whole quite rare,—polydipsia appears to be the initial manifestation of the disease. In one case the patient was observed to develop an *intense thirst* as the initial symptom after a fall on the head. Such observations as these lend support to the idea that there exists a *nervous* form of thirst. They are exceptional, however.

The important rôle played by disturbances of the internal secretions in the pathogenesis of many diseases, and, in particular, of diabetes mellitus, is well known. Sufficient information on this subject is supplied in the works of Sajous, to which the reader is referred. Briefly, a widely held view has been that in most of the cases where a tangible primary disturbance exists the disorder is due to deficient functioning of the posterior lobe of the pituitary body. Even with this conception, however, the matter remains unsettled, experimenters having found that diabetes insipidus could be induced in animals

## DIABETES INSIPIDUS (LÉPINE).

by merely puncturing the hypothalamic region without touching the pituitary body, the conclusion being, therefore, that a lesion of the hypothalamic region, instead of the pituitary, is responsible for this disease.

Hoppe-Seyler (Münch. med. Woch., Nov. 30, 1915) concluded that diabetes insipidus is not due to any one special lesion, but to a vasomotor disturbance from different causes. Kleeblatt's case, in which diabetes insipidus developed after an accident injuring the skull, was mentioned by the same author (Münch. med. Woch., Jan. 11, 1916). Under **pituitary extract**, the polyuria subsided, but the thirst and excessive sweating persisted. The pituitary was found intact, the trouble arising from chronic irritation of the floor of the fourth ventricle.

Indeed, the evidence supplied by the cases published by Camus and Roussy and others, and the experiments of the former in dogs (Endocrinology, Oct.-Dec., 1920), have tended to sustain Sajous's view that there exists a nervous path from the pituitary to the adrenals and kidneys, and that lesions along this path may cause diabetes insipidus or polyuria as well as pituitary lesions.

The disease had long been termed "obscure" or "enigmatic," until the theory sustained by Cushing, Schäfer and Herring and others, that the posterior pituitary body or the pars intermedia produced a secretion, and the observation of Magnus and Schäfer, in 1902, that pituitary extracts caused excessive diuresis, were thought to have established the pathogenesis of the disease on a solid foundation. The labors of Camus and Roussy (1914 and 1920), Houssay and Hug (1921), Bailey and Bremer (1921), and others having shown, however, that an internal secretion of the pituitary body could have nothing to do with the process, since an experimental puncture anywhere in the tuber cinereum could produce the disease, the secretion theory fell to the ground. Its collapse was further insured by the growing opinion that, as first urged by Sajous in 1903 and

later by Biedl (1913) and Swale Vincent (1913), and later voiced at the 3rd International Congress of Neurology by Souques, Alajouanine, Lermoyez and others, posterior lobe preparations, though extremely useful in practice, do not represent a *bona fide* secretion of the posterior pituitary, but merely a pharmacological product or drug. Moreover, unlike these preparations, so effective in diabetes insipidus, the cerebrospinal fluid, which was supposed to contain the secretion, proved quite inert in this disease.

The only remaining theory which meets these experimental and clinical data is that of Sajous, who, in 1907-1908, described 2 nerve paths which, starting in the posterior or neural lobe of the pituitary, passed up by way of the infundibulum to the tuber cinereum, then down the bulb, spinal cord, and splanchnics to the kidneys and adrenals, and submitted evidence to the effect that these pituitarorenal and adrenal nerves governed and sustained the circulatory activity of these organs. Lesions of any kind anywhere in this double path, sufficient to arrest the impulses through it to the kidneys and adrenals (the secretion of the latter contributing to the contractile power of the arterioles), cause passive dilatation of the renal vessels and diabetes insipidus. This accounts for all the phenomena, clinical and experimental, recorded, and also for the beneficial effects of the posterior pituitary products.

**SYMPTOMS.**—The malady may begin insidiously; but it is not unusual for it to appear suddenly, either following one of the causes which we shall name later on, or even without any appreciable cause. It may, in exceptional cases, manifest itself during childhood or infancy.

[I have had under observation a young man 16 years old who was subject to excessive thirst since the first months in his life, the first word he pronounced, at the age of 8 months, being "*water*." R. LÉPINE.]

Case of precocious and hereditary diabetes insipidus in a child of 20 months, in whom the polyuria had begun at 12 months. The mother had had, at various times, periods of marked thirst

and polyuria; her urine was found normal. The child was normal in appearance, except that on the lower jaw it had only the 2 teeth which were present at birth. The urine output was 8 liters a day, the child drinking about the same amount of water. Uranalysis showed: Specific gravity, 1.004; chlorides, 1.1; urea, 1.95; no abnormal constituents. There were no nervous symptoms, nor the least sign of pituitary or neighborhood lesions. The X-ray showed a normal sellar outline. Marañon and Bonilla (*Endocrinol.*, Nov.-Dec., 1925).

Case of diabetes insipidus in a boy of 15 years. At the age of 7 years he had had a brief attack of cerebrospinal meningitis complicating measles, which is thought to have injured the tuber cinereum. Influenza of a nervous form at 14 appeared to have awakened the latent disease in the tuber cinereum, bringing on the manifestations of diabetes insipidus. Sabrazès (*Revue franç. d'endocrinol.*, Feb., 1926).

Thirst and polyuria are the predominating symptoms of the affection. The urine is abundant, usually very pale in color, and is slightly acid. Its specific gravity varies from 1002 to 1010. Consequently, the organic and inorganic principles are not present in any great quantity, but, taking into account the daily amount of urine, it will be found in a certain number of cases that the total quantity of organic and inorganic substances usually considerably exceeds the normal average. With regard to the relative proportions, the chlorides are increased.

In inducing unilateral polyuria in a dog, for instance, by severing a splanchnic nerve, I have observed the production of a relative increase of the chlorides.

The quantity of urine voided during the twenty-four hours naturally bears a certain relation to the quantity of

fluid ingested. As the cutaneous perspiration is usually greatly diminished in diabetic patients, there is, as a rule, less difference between the quantity of fluid taken and that of the urine than in the normal state.

It is even possible that, in exceptional cases, the quantity of fluid taken in one day may be less than that of the urine voided during the same period of time.

In explanation of this paradox there are three hypotheses:—

The first (which is the most natural) is the supposition that during this period the organism becomes impoverished as to water. This hypothesis agrees with several conditions sometimes noticed in polyuric subjects, particularly the increased specific gravity of the blood; if this explanation holds, the weight of the patient should be less during the period in question.

The second hypothesis, which, though not based on any positive fact, does not seem irrational, premises that there is a much greater formation of water in the economy than under normal conditions. In this case, there should be a diminution in the respiratory quotient  $\frac{\text{CO}_2}{\text{O}}$ . If there is more water formed, there is less  $\text{CO}_2$  exhaled. It has been estimated that in a polyphagic individual 100 to 200 Gm. ( $3\frac{1}{2}$  to  $6\frac{2}{3}$  ounces) of water may be produced in the twenty-four hours in this way.

The third hypothesis appears to be less plausible. It consists in the supposition that the economy may absorb, particularly through the lungs, a certain amount of water vapor. It is well known that in the healthy subject copious ingestion of water is

followed, during the two consecutive hours, by the loss in the urine of the greater part of the water taken. This is not the case in diabetes insipidus; the elimination is less rapid, either because the kidney has partially lost its functional elasticity, which enabled it in the normal state to free the blood from an excess of water, or rather because the economy, being, relatively speaking, deprived of water, takes up a certain portion of that ingested.

In the same connection it may be noted that in the polyuric subject the difference existing in the healthy person between the urine secreted in the twelve hours of the day and that of the night is not noticeable.

In a few cases of diabetes insipidus—naturally, the most grave ones—it has been observed that the ingestion of a large amount of sodium chloride does not increase the concentration of the urine. The only effect produced is an augmented urinary output, owing to the excretion of a larger quantity of water. These cases are thus characterized by an *inaptitude to concentration of the urine*, even though there be an excess of salts in the blood. Such cases are, however, rather rare.

Falck advanced the opinion that absorption is retarded in polyuric patients. This supposition is, on the whole, not very likely, but I would say that the dilatation of the stomach sometimes observed in such patients might confirm it in certain instances.

Thirst is a very marked symptom, which, in certain exceptional cases classed under the head of polydipsia, is the original symptom. This point will be again referred to under the head of Diagnosis.

The digestive function is impaired in polyuric patients. This is readily understood, the digestion being disturbed by the ingestion of a large quantity of water, which dilutes the gastric juice. Constipation usually exists.

The sudatory function is almost always abolished. In several patients the fact has been noticed that pilocarpine is incapable of bringing about sweating. Owing to this inability to perspire, it sometimes happens that during great heat in the summer the temperature of these patients rises to 38.5° C. (101.3° F.) and even to 39° C. (102.2° F.). This hyperthermia is not accompanied by malaise.

The insensible perspiration is nearly always greatly diminished,—most frequently reduced to one-half the normal amount,—but sometimes almost abolished. This contributes to the explanation of the fact, already referred to, that the patient excretes as much fluid as he ingests.

Exceptionally, patients have been observed to show copious sweating. The occurrence of this is accompanied by a subjective sense of betterment in the general condition.

An equally interesting phenomenon which has been noticed in a very few cases is an abnormal flow of saliva. Külz observed this complication for a time in a young hysterical subject, and was able to collect, in one day, more than 1 pint of saliva. It is known that physiologists have, during their experiments, sometimes observed salivation in dogs after lesions of the medulla oblongata, etc. In some cases the pulse is slow, and there is also a certain relation between this slowness of the pulse and the increase of the polyuria.

The blood is sometimes *more concentrated* than in the normal state, but this is a quite exceptional condition.

**COMPLICATIONS.**—Complications referable to the nervous system are often met with in cases where the polyuria is itself of nervous origin. These morbid phenomena are merely concomitant, not depending upon the polyuria, but upon its cause. Such manifestations are, *e.g.*, headache, vertigo, neuralgic pains, vomiting, etc. As partly dependent, on the other hand, upon the polyuria may be considered such nutritive disturbances as find their expression in emaciation, coming on even though the patient is polyphagic. It is certain that the excessive washing out to which the tissues are subjected is a cause of exaggerated waste. The presence of inosite in the urine has occasionally been observed. This has been explained as being the result of excessive flushing out of the organism.

**DIAGNOSIS.**—This usually presents very little difficulty. The absence of abnormal principles in the urine indicates by exclusion the existence of simple polyuria. It may happen, however, that the diagnosis between this condition and that of interstitial nephritis gives some little trouble. In certain cases of the last-named affection albuminuria may not exist during a certain period. On the other hand, there are cases of polyuria in which, without any actual nephritis, traces of albumin may be found in the urine.

However, when interstitial nephritis exists, certain uremic symptoms, hypertrophy of the heart, or some one of the symptoms of Bright's disease, are always present. Besides searching for the symptoms of uremia

(cephalalgia, dyspnea, etc.), it should also be remembered that a patient suffering from Bright's disease retains nitrogen in his blood—increase of the non-protein nitrogen—and eliminates less nitrogen in his urine than polyuric patients, and that the urine frequently contains casts. In view of these characteristics, it is generally easy to establish a diagnosis.

How is primary polyuria to be distinguished from primary polydipsia?

In polydipsia thirst is unquestionably the first symptom; it is not preceded by frequent micturition. Polyuric patients do not perspire; in polydipsia perspiration is likely to occur. In the latter affection the quantity of urine does not equal the quantity of liquid ingested; so that, if the patient refrains from drinking during several hours, there will be during this time a diminution or even an arrest of the excretion of urine.

Patients with primary polydipsia display, according to E. Meyer, the normal power of eliminating a concentrated urine after increased intake of salts, which is not the case in diabetes insipidus. In the latter, furthermore, the concentration of the urine is much more constant and the substances in solution are eliminated much more promptly and regularly. Theocin raises the concentration in diabetes insipidus without increasing the amount of urine.

Case of a woman aged 31, congenitally syphilitic, who had had hemiplegia 7 years before, and for 5 years had experienced diabetes insipidus and marked obesity without any clinical or X-ray evidence of pituitary tumor. Lumbar puncture had no effect. Pituitary extract hypodermically greatly reduced the polyuria and also decreased the adiposity. The writers consider this a case of true pituitary diabetes insipidus. The condition is of pituitary origin when attended with other pituitary symptoms, unaffected by lumbar puncture, and reacting to organotherapy; it is of nerv-



ous origin when there are symptoms of basilar meningitis, with altered cerebrospinal fluid, when lumbar puncture affects the polyuria, and when pituitary treatment is ineffectual. Gilbert, Villaret and Saint-Girons (*Revue neurol.*, June, 1922).

Hypo- and hyperchloremic types of diabetes insipidus differentiated. The former shows a high basal metabolism, which declines markedly under restriction of fluids and, especially, **atropine** therapy. The hyperchloremic type shows a normal or low metabolism, reacts to restriction of fluids with loss of weight and serious symptoms, and is not affected by atropine. The hypochloremic type differs from polydipsia in the low serum chloride content, chronic ingestion of excess of water causing a hyperchloremia. Veil (*Deut. Arch. f. klin. Med.*, Dec., 1925).

**TREATMENT.**—The injection of **pituitary posterior lobe extract** is probably the most satisfactory method of treatment. Although disquieting symptoms may attend its use in this manner, they seem to be temporary.

In a case of diabetes insipidus 2 c.c. (32 minims) of **pituitrin "O"** given intramuscularly during a 24-hour period reduced the polyuria and raised the salt and urea nitrogen content of the urine. The effect began in 10 minutes, and after a 1 c.c. dose lasted 8 to 12 hours: The urea nitrogen, uric acid, and sugar in the blood were almost doubled within 3 hours. The drug enabled the kidney to excrete a larger amount of phenolsulphonphthalein. D. S. Hachen (*Amer. Jour. Med. Sci.*, June, 1923).

In 37 cases treated at the Mayo Clinic, consistently good results were obtained only from frequent subcutaneous injections of **posterior pituitary extract**, though in a few, considerable effects followed its intranasal use as a spray, instilled into the nostril by a medicine dropper, or applied on a pledget of cotton. When obstetrical pituitary extract was not sufficiently effective, the surgical extract proved

more satisfactory. Rectal administration was sometimes helpful, but only for short periods, usually 2 to 4 hours. **Spinal puncture** in 19 cases yielded only moderate reduction of symptoms for 2 or 3 days in 2 or 3 cases. In cases secondary to neoplasm, **operation** should be considered on its own merits, without reference to the diabetes insipidus. Much can be accomplished in allaying the patient's apprehension, especially in idiopathic cases, by assurance that he has nothing more to fear than the discomfort and inconvenience of the disease. Of 36 cases, 8 died, 3 were cured, 8 were definitely improved, 9 unchanged, 5 continued daily injections, and 8 were untraced. Rowntree (*Jour. Amer. Med. Assoc.*, Aug. 9, 1924).

There is little chance of a cure unless very large doses of **pituitary extract** are given. The treatment can be continued for months without toxic effects. Intravenous administration should be avoided, as it may induce fatal collapse. The writer observed good results from the daily ingestion of 7 **fresh beef pituitaries**. K. Motzfeldt (*Norsk Magazin f. Laeg.*, Sept., 1924).

Sajous found that all untoward symptoms of the posterior pituitary treatment could be avoided and equally good results obtained as with injections, by giving **pituitary**,  $\frac{1}{10}$  grain (0.0065 Gm.), together with **ergotin**, 1 grain (0.065 Gm.), in a capsule three times daily after meals.

Case of polyuria in a man of 73 years, shown to be renal in origin by the high nitrogen content of the urine and by Ambard's coefficient. Lumbar puncture yielded no benefit, while daily injection of pituitrin controlled the polyuria transiently. Thus, pituitary medication is not specific for diabetes insipidus, but may be classed as a procedure of general therapy. J. Lhermitte (*Revue neurol.*, June, 1922).

A **pituitary tartrate**, or new preparation of the active principle of the posterior lobe, used in 4 cases of dia-

betes insipidus, with results similar to those obtained with the ordinary pituitary products. The preparation is effective by the nasal route in a dosage of 4 drops of a solution of 0.5 mgm. ( $\frac{1}{30}$  grain) per c.c. (16 minims) of water in each nostril every 3 hours. J. J. Abel and E. M. K. Geiling (Jour. of Pharm. and Exp. Ther., Nov., 1923).

The benefit from **posterior pituitary** preparations is accounted for, not by a supposed secretion or hormone in these products, but by their recognized pharmacologic property of causing constriction of the arterioles, thus counteracting in the kidneys the dilation of these vessels, which dilation is the cause of diabetes insipidus and polyuria insofar as their relationship with the hypophyseorenal nerve path is concerned. C. E. de M. Sajous (Amer. Jour. Med. Sci., May, 1924).

In 2 cases of diabetes insipidus no benefit resulted from insulin treatment, with or without addition of calcium, potassium, or sodium ions. Addition of insulin did not seem to enhance the prompt benefit from **pituitary extract**. Waldorp (Rev. de la Assoc. méd. Argent., Dec., 1925).

In neuropathic subjects the general condition should be treated with **potassium bromide**, **valerian**, and especially **strychnine**, which has yielded very gratifying results. De Ketly, *e.g.*, witnessed partial or complete recovery in three out of four cases under strychnine, begun in  $\frac{1}{120}$  grain (0.0005 Gm.) doses, then gradually increased.

Where the foregoing measures fail, **ergot** (or, even better, **ergotin**) and **antipyrin** should be tried. Fontana and others have noted pronounced benefit from **atropine** in ascending doses. **Mercury** and **neoarsphenamin** have given good results in cases with a positive Wassermann reaction.

Two cases of clinical recovery under **antisiphilitic treatment**, although

the Wassermann was negative. Slight changes suggesting neurosyphilis were found in the cerebrospinal fluid. Castellano and Schteingart (Prensa méd. Argent., Mar. 20, 1924).

First case on record treated by **X-ray** exposures of the pituitary. Early pituitary tumor was diagnosed on account of a constant visual field defect in the right upper temporal quadrant. Eleven series of X-ray cross-fire treatments in a year resulted in return of the visual fields to normal, drop of the urine output to 2.5 liters—at which it had remained over 3 years,—and transformation of a totally incapacitated man into an efficient wage-earner. E. B. Towne (Jour. Amer. Med. Assoc., Dec. 27, 1924).

I have obtained some success by the use of the **continuous current**, the positive pole being placed upon the spinal column, and the negative at the level of the hilum of the kidney.

When patients are able to stand without too much distress a limitation of the intake of fluid, this **restriction** should be imposed; in the grave cases, however, this is absolutely impossible of realization.

In a few cases some betterment has been experienced through the use of **diaphoretic measures**.

**Lumbar puncture** has sometimes been resorted to, but the results have not been conclusive.

R. LÉPINE,  
Lyons.

**DIABETES MELLITUS.—**  
**DEFINITION.**—A disease characterized by non-accidental—*i.e.*, permanent or very nearly permanent—glycosuria, associated with hyperglycemia, and attributed to disease of the islands of Langerhans.

**ETIOLOGY.**—The incidence of diabetes varies to a great extent in accordance with the factors of age.

race, occupation, etc. It is not the same in different countries. All that can be said, in a general way, is that diabetes is not a rare affection. The statistics put forth by Williamson show, indeed, that different countries are very unequally afflicted with it. Among the different cities of France there is a singular divergence in the incidence of diabetes; thus, by comparison with Bordeaux, the disease is relatively rare in Lyons.

The mortality-rate from diabetes is higher in New York City than in Philadelphia. The average death-rate per 100,000 of population rose steadily from 4.1 in the 5-year period 1880-84 to 21.4 in the period 1920-24. In Philadelphia the corresponding figures were 3.4 and 17.0. Whereas, in 1913, diabetes occupied twenty-second place among the leading causes of death in Philadelphia, in 1923 it has risen to twelfth place. For the Registration Area of the United States in 1920, diabetes likewise appeared in twelfth place. Insulin checked the further rise in the death-rate during the last half of 1923 and during 1924 in Philadelphia. A phenomenal rise in the diabetic deaths in females has been taking place. In 1924, in Philadelphia, there were 229 deaths in females to 116 in males. Since 1903, in this city, the deaths among females have exceeded those among males. J. M. Anders and H. L. Jameson (*Amer. Jour. Med. Sci.*, Sept., 1925).

The relative frequency of diabetes mellitus in middle age and in the period of decline is well known. Below the age of 30, on the other hand, and especially in childhood, it is relatively uncommon. The dominant cause of diabetes in childhood is an inherited tendency.

Men are, in general, more likely to be attacked by diabetes than women. Cantani reported that, out of 1004

cases, 837, or 83.37 per cent., were males, and 167, or 16.63 per cent., were females. This difference is, however, somewhat excessive and is not reproduced in other statistics.

The proportion of males and females in the white race who suffer from diabetes is about 3 to 2. In children, however, the ratio is not the same; girls have it somewhat more frequently than boys. According to Fitcher, in the colored race the cases occur more frequently in women than in men. In the same country different races are very unequally affected, and on this point, too, it is necessary to await further investigations.

The prevailing belief at the present time is that diabetes occurs with relative frequency in the Jewish race. Wallach found that, out of 156 persons who died from diabetes, 51 were Jews and 105 belong to other denominations. The mortality from diabetes is six times as great (according to this author) among Jews as it is in other religions. The correctness of this conclusion has, however, been challenged by Pollatschek.

Statements concerning the morbidity of Jews in relation to diabetes mellitus are of little value, according to Pollatschek, as there is never any statement as to the relative number of Jews and Christians in the clientele of the reporter. The writer treated 4714 persons, 2381 of whom were Christians and 2333 Jews. There were 653 diabetics, 289 of these being Christians and 364 Jews; *i.e.*, reckoned by the number per thousands of all patients, 124 Christians and 155 Jews had diabetes. Moreover, diabetes is common in England, where there are few Jews.

In a study of the mortality of diabetes mellitus in 1775 subjects, the writer found that the ratio of deaths from diabetes to the total number of deaths from all causes was 0.018

among Jews and 0.007 among non-Jews. Morrison (Boston Med. and Surg. Jour., July 13, 1916).

Anders and Jameson found that out of 345 deaths from diabetes in Philadelphia in 1924, the greatest mortality occurred after the 60th year—188 cases, against 120 between the ages of 40 and 59, inclusive; 26 between 20 and 39, and 11 below 20 years.

Diabetes is frequently hereditary, inasmuch as several members of one and the same family are often affected.

Case of a diabetic Jew aged 35 years, whose 3 sisters had died in diabetic coma at 17, 19, and 23 years, respectively. In each the illness lasted only a few months. The mother had died in diabetic coma at 32, after 2 years' illness. Her brother and 1 sister had died in coma at about 40, and her other sister, in her fifties, was also diabetic. None of the patient's father's family were diabetic. Kern (Atlantic Med. Jour., Jan., 1926).

The influence of heredity is much greater than that of race,—a fact which is not surprising, the component units of a race being much less like to one another than those of a single family. The factor of inheritance is observable in one-fifth of all cases. That which is inherited, however, is not so much the disease itself as the predisposition to it, since rather frequently diabetes appears in the offspring before it has become manifest in the father.

An inherited predisposition was recorded by Frerichs in 10 per cent. of 400 cases; Külz, 25 per cent. of 592 cases; Naunyn, 17 per cent. of 398; von Noorden and Williamson, about the same percentage. Schmitz found a history of diabetes in other members of the family in 47 per cent. of 2115 cases. Heiberg found only 7 relatives with diabetes among 100 non-diabetics, as against

18 among 100 diabetics. The diabetes had set in before the age of 10 in 7 of the 100 cases and between 10 and 20 in 18.

The frequency of demonstrable hereditary cases cannot as yet be stated, on account of insufficient investigation of the matter, but it is evidently greater than has been suspected. Inadequacy of the islands of Langerhans, now known to be the cause of the disease, can be inherited, and may be due to numerous factors. Hansen (Acta med. Scandinav., Apr. 1, 1925).

It has been observed that obesity, gout, and neuropathic affections exist with unusual frequency in diabetic families (Prout, Bence-Jones, Bouchard). Frequently obesity and diabetes coexist in the same person. A too abundant diet and the abuse of wine and cider are predisposing causes of diabetes. In 607 persons engaged in manual labor or requiring great muscular and respiratory activity whose urine was examined by Worms, no sugar was found in any instance; in 100 persons engaged in intense intellectual work, sugar was found in 10—a proportion which appears to me exaggerated.

Statistical inquiry into the predisposing influence of obesity in diabetes mellitus, based on 1306 cases of obesity and 145 of diabetes, all personally observed. The average percentage of overweight in diabetics was 21.62 among Gentiles and 27.55 among Jews. The incidence of diabetes among obese Jews is higher than among obese Gentiles in a ratio of 12 to 8. While adiposity does not *per se* explain the marked rise in the prevalence of diabetes in the female in recent years, it is the most potent single predisposing factor in this disease. As is well known, the chief cause of adiposity is the ingestion of foods containing a large percentage of carbohydrates. Anders and Jameson (Amer. Jour. Med. Sci., Sept., 1925).

The causes which we have mentioned so far are *predisposing* causes.

**Determining Causes.**—As to the *exciting* causes of diabetes, acute infectious diseases can be considered in this category, for the affection sometimes comes on after typhoid fever, eruptive fevers, etc., and especially after influenza. With regard to malaria, several French physicians have noted a temporary glycosuria after attacks of intermittent fever; but in malarial countries true diabetes does not appear to be any more common than elsewhere. The importance of syphilis has also been exaggerated.

In 73 sera received from patients with a known history of diabetes, almost all were chylous, many of them extremely so. This is common in sera from diabetics, the fat content of the serum being usually abnormal. Only 1 serum gave a positive Wassermann reaction, 51 were negative, 2 doubtful, and in 19 the serum controls failed to hemolyze, so that no readings could be made. This seems to dispose of the contention that diabetic sera give readable positive reactions with Wassermann antigens when there is no clinical evidence of syphilis. A. I. Van Saun (Jour. Med. Research, xxxvii, 205, 1917).

The writer questions Warthin and Wilson's recent statement that syphilis is a frequent cause of diabetes mellitus. Numerous severe diabetics have a considerable degree of cholesterinemia, and should, therefore, tend to react specially sensitively to the Wassermann test if syphilitic. Historically and on the basis of the Wassermann reaction, syphilis is not commonly associated with diabetes, and a careful examination of the writer's series of 143 diabetics from the point of view of history, suggestive symptoms or lesions, and the Wassermann reaction, showed that only 4 had evidence of syphilis and

all 4 gave a positive reaction to the Wassermann test. J. R. Williams (Jour. Amer. Med. Assoc., Feb. 9, 1918).

Six cases of diabetes developing on the basis of syphilis. In all of them the glycosuria disappeared under anti-syphilitic treatment. Padilla and Paz (Rev. de la Asoc. med. Argent., July-Sept., 1920).

Acute pancreatic diabetes is frequently due to infection of the organ following tonsillitis. The writer reports 4 cases, including 1 with diabetes appearing 2 weeks after mumps; another, 12 days after severe tonsillitis, and a third (with polyuria, polydipsia, and loss of flesh), within a month after severe tonsillitis. Blodgett (Penna. Med. Jour., Mar., 1921).

Case of diabetes setting in 3 months after influenza. No glycosuria had appeared during the acute illness nor the period of convalescence. Examining a specimen of the day's urine passed by other former influenza patients, the writer found sugar in 9 cases. Five of these were cured and remained well. Two died within 3 and 9 months, respectively. Of the remaining 2, 1 died within a year and the other, after some temporary improvement, at the beginning of the third year, of true diabetes mellitus. Apparently, influenza, especially if of gastrointestinal type, is apt to be followed by diabetes, which may not declare itself for several weeks after a seemingly complete recovery from the influenza. Uranalysis is called for in all such cases at intervals for some weeks at least after the influenzal symptoms have subsided. C. E. Shelley (Lancet, Apr. 10, 1926).

The part played by contagion in diabetes is as yet not based upon any very exact observations. The occurrence, said to be quite frequent, of diabetes in husband and wife has been a mooted question. An analysis of 2320 cases by Schmitz gave 26 examples of such occurrence—probably coincidences, according to Senator.

[A feature which is overlooked in this connection is that the same diet is partaken of by husband and wife. In two of Sajous's cases the excessive use of sugar and sweets caused the glycosuria. If, as he states, their mates had also acquired the habit, each couple would have been characterized as suffering from conjugal diabetes in statistical tables, suggesting contagion—obviously an erroneous conclusion.]

Mental shocks, violent emotions, especially of fear, may be the cause of diabetes. Smith and others have emphasized the frequency with which this affection occurs in locomotive engineers. In addition to pronounced emotional stresses and prolonged worry, especially financial worry, grief, such as follows, for example, the loss of a child, also unquestionably exerts a diabetogenic influence in predisposed individuals. According to statistical studies of the question, these various causes are operative in at least one-third of the cases of diabetes.

In a special study of over 100 cases in soldiers, the writer found that only 1 occurred in the reserves, the rest being among soldiers actively engaged at the front. The chief causes seemed to be increased physical exertions combined with poor living conditions and an improper diet. About 65 per cent. occurred in men who had not previously shown signs of diabetes; the remainder had had the disease in mild form or had shown some tendency to it. Proper care and diet usually removed the glycosuria sufficiently to restore the men to less active military duty. The most important index was the state of the blood-sugar. If this remained high after treatment the prognosis was not so favorable as if it fell fairly promptly to normal. C. von Noorden (*Med. Klinik*, Sept. 17, 1916).

Many other etiological factors might be mentioned. Thus, in some instances

diabetes is observed to appear during pregnancy or after the early cessation of lactation. Cases have been reported, on the other hand, in which the phenomena of the disease ceased during a part at least of the gestation period. These various occurrences may be fairly well accounted for when one tries to analyze them. Thus, in the last-mentioned instance, it is with women whose nutritional processes have been slowed and who were eating to excess that one has to deal. The growth of the fetus has been of benefit to them in that it eliminated for them an excess of nutritive material.

**Traumatic Diabetes.**—According to my personal statistics, 5 out of every 100 diabetics have been the victims of trauma. Cantani would place the ratio at twice that mentioned, but in my opinion such an assertion is greatly exaggerated, especially in the adult. Perhaps it can be sustained, however, in children, since falls on the head are very common among them.

A traumatic factor was found by the writer in 2 per cent. of 4068 cases of diabetes. Cantani's 1004 cases even showed 10 per cent. As a rule, the glycosuria following trauma does not go on to true diabetes, but disappears after about 2 years. Ferrannini holds, however, that diabetes may be caused by trauma in persons who have not the slightest predisposition to it. The question whether diabetes following trauma is caused by the injury or is merely an awakened latent diabetes is of no great medicolegal importance, as the patient is entitled to damages in either case. Diabetics should not be assigned to work which exposes them to traumatism. S. Diez (*Policlinico*, Mar. 28, 1921).

Trauma of the skull is particularly effective as a cause of diabetes. It

must be clearly kept in mind, however, that the knowledge of a previous traumatism does not necessarily imply that the diabetes present is of traumatic origin, for in a certain number of these patients the existence of an inherited predisposition may be noted. In such instances traumatism acts only as an accidental cause.

A study of 212 cases of traumatism of the head admitted into the Boston City Hospital within thirteen months showed five classes: (1) Wounds of the scalp; (2) wounds with denudation of the bone; (3) comminution, including cases followed by loss of consciousness, but without fracture; (4) fracture of the vault; (5) fracture of the base. F. A. Higgins and J. B. Ogden found that of the first class there were 84 cases, 5 of which, or 6 per cent., presented glycosuria; in the second class, 43 cases, 4 with glycosuria,—9 per cent.; third class, 40 cases, 1 with glycosuria,—2.5 per cent.; fourth class, 24 cases, 5 with glycosuria,—20.8 per cent.; fifth class, 21 cases, 5 with glycosuria,—23.8 per cent. In all there were 20 cases of glycosuria in 212 cases.

Among 100 cases of traumatic diabetes, a more or less severe lesion of the floor of the fourth ventricle was found in approximately 25 cases, various lesions of the central nervous system in 40, and no discernible lesion in 35.

Through the advances being made in anatomical studies, the last of these categories will doubtless be further reduced. This is all the more probable since, in the absence of all trauma, violent emotion in itself appears to be sufficient to produce a slight lesion (through vasomotor

action). Thus, Williamson reported the case of a healthy young woman who, upon witnessing her nephew sustain a fall, experienced an extreme emotional shock, then remained in a state of anxiety which rendered her incapable of all work. Four weeks later, polyuria and glycosuria were observed; then, symptoms of grave diabetes, from which she succumbed in seventeen months. The autopsy revealed the presence of small hemorrhages in the floor of the fourth ventricle.

Independently of traumatism, there are sometimes found in diabetics, though rather uncommonly, lesions of the nervous system. The number of unquestionable reported cases of spontaneous lesions of the fourth ventricle which had brought on diabetes is relatively small. According to the experiments of Camus, Gournay and Le Grand, glycosuria is particularly likely to occur from a lesion in the walls of the third ventricle; or, an ependymitis, hemorrhage, or a tumor in the third ventricle may act similarly by affecting the paraventricular nucleus.

As for the organic changes (softening, etc.) which may be found in the cerebral hemispheres in diabetics, in some cases proof is available of the fact that they are secondary.

**Lesions of the Pancreas.**—A more or less marked cirrhosis of the pancreas is met with in a large number of individuals, whether diabetic or not. It is quite out of the question to gain an exact appreciation of the etiological value of a pancreatic lesion with the naked eye alone. A histological examination is indispensable, for the microscope alone will permit

of distinguishing the common pathological change, periacinar cirrhosis, from intra-acinar cirrhosis, which process alone offers an obstruction to the elaboration of the internal secretion of the organ.

In 1889, Minkowski and von Mering found that complete pancreatectomy in animals led to a typical diabetes, with coma and death. By this operation the ability of the liver and muscles to lay up glycogen was annulled, even the giving of an abundance of carbohydrates failing to bring about deposition of glycogen in these structures. The blood sugar, however, was above the normal (hyperglycemia). This seemed to show that pancreatectomy removed some substance or function normally assisting in carbohydrate conversion.

In 1900, Opie, and in 1901, Ssoblew developed, on the basis of pathological studies, the view that absence of an internal secretion from the islands of Langerhans is specifically responsible for the appearance of diabetes. These islands or islets, measuring but 0.2 mm. in diameter, and consisting of small polygonal cells with round nuclei, are located mostly in the middle of the externally secreting pancreatic acini, and are scattered through the pancreas, though more plentiful in the tail of this organ than elsewhere. In many cases of diabetes, Opie found an interacinar type of interstitial pancreatitis, with hyaline degeneration and atrophy of the islands of Langerhans, while the cells of the ordinary pancreatic acini were not involved. The fact that not all cases of diabetes show degeneration of the islands is explained on the supposition that their activity may

suffer from a mere functional disturbance, in the absence of any change visible microscopically.

Another step in the elaboration of the evidence favoring the islands as the sole cause of diabetes was taken through the experimental studies of MacCallum, which are summarized by this investigator as follows: "The ligation of the pancreatic ducts results in atrophy of the acini, but since the islands of Langerhans have no connection with these they do not suffer and no glycosuria results. In one type of experiment, half of the pancreas was thus ligated off, and the animal survived perfectly well. After a year such an animal (dog or guinea-pig) showed the complete reduction of the ligated part to a thin, transparent film in the mesentery; extirpation of the remaining intact half of the pancreas was followed in such an experiment by glycosuria, but after one day of this the animal showed no symptoms whatever and could assimilate large amounts of glucose or starch. After a month, the transparent film which represented the other half of the pancreas was extirpated, and then the animal was plunged into the severest diabetes. This film contained only islands of Langerhans."

On these results was based the production by Banting, in 1922, of insulin, constituting an active anti-diabetic principle derived from the islands of Langerhans. The therapeutic effects of this principle would seem to afford additional evidence of the importance of the islands in the production of diabetes; yet, neither MacCallum's experiments nor insulin can be said completely to prove that changes in the islands are the *sole*



cause of diabetes, since they do not exclude a participation of disease of the remainder of the pancreas in the process. It may be noted, in this connection, that the cells of the pancreatic acini and those of the islands are of identical origin and of like nature. It appears quite possible, therefore, that the first-named may yield some principle to the lymphatic or blood-capillaries. Personal researches showed, indeed, that the primary effect of ligation of the duct of Wirsung is to augment greatly the glycolytic power of the blood. Since the islands of Langerhans are not in communication with the excretory ducts, an excessive pressure in the latter can react only upon the cells of the acini.

Autopsy records of 90 cases of diabetes, special attention being paid to the lesions in the pancreas. There were found:—

(1) *Chronic inflammation of the pancreas.*

CASES.

Interacinar pancreatitis; sclerosis of the islands of Langerhans .....	39
Interlobular pancreatitis; sclerosis of the islands of Langerhans .....	4
Interacinar pancreatitis; hyaline degeneration of the islands of Langerhans .....	19
Interacinar pancreatitis with lipomatosis; sclerosis of the islands of Langerhans .....	2
Interacinar pancreatitis with siderosis of the islands of Langerhans (hemochromatosis) .....	2
(2) <i>Parenchyma normal; lesions of the islands of Langerhans.</i>	
Sclerosis of the islands of Langerhans .....	4
Hyaline degeneration of the islands of Langerhans .....	7
Infiltration of leukocytes about the islands of Langerhans .....	1
(3) <i>Pancreas normal</i> .....	11

Of the 11 cases with a normal pancreas 5 showed marked diminution in the number of islands of Langerhans. In 5 other cases the pancreas was abnormally small.

These lesions are not secondary to diabetes, but are primary, as shown by the variety of lesions found. The essential cause of pancreatic diabetes is a lesion of the islands of Langerhans because, as the case analyses show, lesions of the islands with normal parenchyma often occur, while many cases of interlobular pancreatitis without lesions of the islands occur in cases of duct obstruction without any signs of diabetes having been present during life. Cecil (Jour. of Exper. Med., March 1, 1909).

The microscopic diagnosis of diabetes is satisfactory. In no case did the writer find a strictly normal pancreas. The diabetogenic lesions are acute pancreatitis, specific lesions of the islands of Langerhans, general fibrosis, and scarcity of islands. The island lesions are the most suggestive, including fibrosis, alone or with hyaline degeneration. Even when visible changes are slight, the fundamental damage may suffice to cause diabetes. General fibrosis is the commonest change. Scarcity of islands may result from inflammatory or toxic destruction or from hydropic degeneration. The latter is the one anatomic effect of diabetes, explaining the irreparable lowering of assimilation and demanding thorough dietetic control. Vacuolation is the sign of intense functional exhaustion, and goes with intense activity of the diabetic process, occurring most often in coma and in severe cases, but not in the mild cases under dietetic control. F. M. Allen (Jour. of Metab. Research, Feb., 1922).

In 6 out of 26 cases of diabetes the islands appeared less numerous than in normal pancreases. In 13 hyalinization of the islands was found; in but 1 of these was the patient below 45 years of age. Five showed more or less sclerosis of the islands. In 5 there was some lymphocytic infiltra-

tion about scattered islands. In 4 there was no demonstrable pathologic change in the islands. In 3 the islands showed Cecil's adenomatous type of enlargement. There was no pancreas without some apparently normal islands, no matter how severe the clinical features or the changes in some of the islands. The acinar tissue showed varying sclerosis independently of changes in the islands. With 2 exceptions, acinar sclerosis was not apparent in any case much under 2 years' duration, even though the islands showed considerable change. No correlation between diabetic coma and pathology was found.

The variation and inconstancy of the pancreatic lesions argue against an infectious origin of the disease. The cause seemingly acts over a long period. The autopsy changes in the pancreas represent rather the result of a long struggle between the regenerative activity of the pancreas and the degenerative changes caused by the diabetogenic factor. Evidence of the power of the pancreas, and of the islands in particular, to regenerate after acute injury is easily obtained. Temporary injury to the islands may explain the severe drop in sugar tolerance noted in diabetics during acute infections. H. F. Root and S. Warren (Boston Med. and Surg. Jour., Jan. 14, 1926).

That the islands of Langerhans are not the exclusive source of the internal secretion of the pancreas is suggested by the fact that in many instances of diabetes no universal destruction of the islands is present. Frequently there is found instead a fine scarring of the organ analogous to cirrhosis of the liver, or sometimes no recognizable change at all (MacCallum). The matter seems further complicated in that in some destructive lesions of the entire pancreas, glycosuria fails to appear. Thus, in acute hemorrhagic pancreatitis with

destruction of the organ, glycosuria is rare (this has been explained as due to the prompt fatal termination usually occurring in such cases), while in extensive cancer of the pancreas glycosuria has been noted in only a small proportion of cases. According to Fletcher, the failure of diabetes to develop is explainable in that the islands are more likely to be preserved at least partly intact than the acinar portion of the pancreas.

The writer questions the independence of the islands of Langerhans and the conception of them as organs of internal secretion essential for the combustion of sugar. The islands are embryologically derived from the same cells as the rest of the parenchyma. They can, by serial sections, be shown to have intimate connection with the parenchyma and even with the ducts. In older subjects groups of acini may take on the appearance of islands, and typical acinar cells and transition to acinar arrangement are sometimes seen in islands. Additional evidence is adduced to show that the islands are really interchangeable with the parenchyma, and constitute a phase in the constant morphologic fluidity of the pancreas. After experimental duct ligation, causing extensive cirrhotic loss of pancreatic substance, it is often possible to trace the formation of apparent remaining islands through various stages back to atrophying acinar cells. With von Hanseemann, Herxheimer and Reitmann, the writer recognizes the importance of the pancreas in its relation to metabolism, not in a particular secretion of the islands of Langerhans, but in activity of the whole organ. Büchner and Grafe's investigation has pointed towards insulin action as a general cell function. Insulin having been found generally in glands and tissues other than the pancreas, some observers lean toward the view that the latter organ is merely a storehouse for insulin. Horst Oertel (Lancet, Apr. 5, 1924).

**Other Internal Secretions.**—The internal secretion of the thyroid gland and especially that of the adrenals tends to increase the amount of sugar in the blood. It has even been asserted that the latter is indispensable for the production of a hyperglycemia.

[See on this point Dr. Sajous's work on the "Internal Secretions," Vols. I and II. The reader will find therein a discussion of all the details of the subject, which cannot be given here. In Sajous's opinion, advanced in the above volumes (1903-1907), both the adrenals and thyroid, when overactive, can produce diabetes by inducing, through their secretion, abnormal oxidation and metabolism in the pancreas. The latter organ being thus caused to produce an excess of amyl-opsin, which in turn acts on the hepatic glycogen, sugar is formed beyond the needs of the tissues at large, and the surplus of sugar is eliminated with the urine. This he terms the *sthenic* form of diabetes mellitus. In what he terms the *asthenic* form, the adrenal and thyroid are insufficient and, metabolism in the pancreas being correspondingly impaired, alimentary glycosuria occurs precisely as it does after removal of the pancreas or to a less degree when disease of the pancreas inhibits its functional activity. R. LÉPINE.]

Intravenous injection of adrenalin induces glycosuria, probably through increased mobilization of glycogen in the liver, formation of an excess of glucose, and resulting rise in the blood sugar. Increased activity of the chromaffin tissues seems to exert an "accelerator" influence on carbohydrate metabolism, antagonizing, in this respect, the pancreas, which is thought to inhibit glycogenolysis (*i.e.*, the conversion of glycogen into glucose). On this basis, the various causes of sympathetic overactivity are capable, acting through the adrenal secretion, of inducing glycosuria by upsetting the normal balance be-

tween the adrenal and pancreatic functions. Diabetes of adrenal origin could occur only in hyperadrenia, and is therefore not observed in organic adrenal diseases, which reduce adrenal activity; on the contrary, *hypoglycemia* follows bilateral adrenalectomy and occurs in Addison's disease, accounting for the muscular weakness in the latter condition.

Adrenalin, 0.5 c.c. (8 minims), injected in fasting infants, induced a transient diabetic acidosis with hyperglycemia, glycosuria, and ketonuria. Ammonium chloride checked this action and reduced the glycemia, glycosuria, and ketonuria. Conversely, sodium bicarbonate, even in dosage sufficient to alkalinize the urine, failed to prevent the adrenalin acidosis. Beumer (Zeit. f. Kind., June 7, 1923).

A possible influence of the thyroid in diabetes is suggested by the fact that in thyroid hyperactivity, as in exophthalmic goiter, carbohydrate tolerance is reduced, while in hypothyroid states it is markedly increased. In exophthalmic goiter, glycosuria and even true diabetes sometimes occur. The glycosuria following pancreatectomy is reduced by thyroidectomy, and in dogs subjected to the latter operation, according to Falta, adrenalin fails to induce glycosuria.

A marked influence of the pituitary on carbohydrate metabolism is likewise well known. Cases of diabetes dependent upon a tumor of the pituitary, generally but not always with concomitant acromegaly, are known to occur. Insufficiency of the posterior lobe results in a very striking increase of carbohydrate tolerance. Conversely, injection of posterior lobe extract in dogs has been found to induce glycosuria and in-

crease of blood sugar. Glycosuria in pregnancy and after basal fractures has been ascribed to a stimulation of the posterior lobe of varying duration.

Almost constantly in younger individuals, but much more rarely in older subjects, the author finds a reduced weight of the pituitary body, seemingly due to diminution of the size of the anterior lobe, with reduction in number and size of the eosinophile cells and sometimes degenerative changes in these cells. True diabetes is to be regarded always as pancreatogenetic, but aside from the pancreatic disease, whether true diabetes will develop depends largely on the condition of the other organs concerned in sugar metabolism. In normal subjects with these other organs unimpaired, severe pancreatic changes are necessary if diabetes is to result, whereas much less severe changes are required in persons in whom the glands that aid in sugar formation and are antagonistic to the pancreas are hyperactive, *e.g.*, the pituitary in acromegaly and the thyroid in exophthalmic goiter. Similar considerations apply in individuals in whom from any cause there is organically or functionally induced irritation of the nerve centers or pathways of the mechanism governing sugar metabolism. Kraus (Arch. f. path. Anat., cclxvii, 1, 1923).

It is quite certain that disorders of various internal secretions may favor the development of diabetes. Apert, Spillmann, Jeandelize, and Parisot have, among others, reported cases of diabetes which appeared to depend upon an infantilism of endocrin origin. The internal secretions are subject to influences of the nervous system, and diabetes may be, in a certain number of cases, dependent upon an excitation of the sympathetic overbalancing the influence of the antagonistic (autonomic) nerves.

In a case of diabetes with intense hyperglycemia, there was a sarcoma

enveloping the pancreas, but no invasion of the organ itself by the tumor. The abdominal sympathetic was, however, embedded in the latter, and the writers deduce from this a sympathetic origin of diabetes, involving a relationship to the endocrine glands. Dufour, Rouèche and Baruk (Bull. Soc. méd. des hôp. de Paris, July 25, 1924).

The fundamental cause of diabetes is excessive excitability of the splanchnic sympathetic. Vasoconstriction of the liver capillaries results, with hypotension of the interstitial plasma and withdrawal of glycogen from the interior. The effect of insulin can be reproduced by almost any vagotropic substance. In clinical cases glycosuria was greatly reduced or dropped to zero upon intramuscular injection of 2.5 Gm. (38 grains) of peptone. Pimenta Bueno (Brazil-méd., July 18, 1925).

**Lesions of the Liver.**—Owing to the views of Claude Bernard, much attention has been given to the condition of the liver in diabetes. In most instances, however, this organ has been found normal *post mortem*; in one-third of the cases, slightly enlarged. In rare instances a more or less cirrhotic state of the liver is discovered. When this condition is present, microscopic examination shows that the pancreas is also cirrhotic. According to Jones, Castle, Mulholland and Bailey, one-fifth of all diabetics over 40 years of age have an associated cholelithiasis.

Hanot and Chauffard, Letulle, and others have called attention to the possible simultaneous presence—which is, however, rare—of a cirrhosis of the liver, generally hypertrophic, of a more or less generalized pigmentation, and of diabetes. To this combination of phenomena has been applied the term *bronzed diabetes*. This has been shown to be a late stage of

*hemochromatosis*. Owing to the extensive deposition of hemosiderin in the pancreas, the latter becomes the seat of pronounced interstitial pancreatitis, from which the diabetes is believed to result.

**PATHOGENESIS.**—The monosaccharides produced by digestion of the ingested carbohydrates consist mainly of dextrose (glucose), together with small amounts of levulose and galactose, and upon reaching the liver through the portal vein are converted therein through a process of dehydration into glycogen. The re-conversion of glycogen into dextrose (glycogenolysis) to satisfy demands of the body for energy-yielding pabulum is believed to be brought about by a diastatic ferment known as glycogenase, which occurs in extracts of liver and of some other tissues (*e.g.*, muscle glycogenase) as well as in the blood and lymph.

The dextrose thus set free from the liver glycogen is carried in the bloodstream to the muscles and other tissues, where it is consumed, with liberation of heat and energy. While the decomposition of the dextrose eventually yields carbon dioxide and water, the dextrose molecule is not supposed to undergo direct oxidation, cleavage and other intermediary reactions, concerning which little is as yet known, intervening.

Hyperglycemia, the essential phenomenon of diabetes mellitus, is itself the result of a diminution of the power of the tissues to consume dextrose (glycolysis). Diminution of glycolysis to a greater or less extent exists in all diabetics. This deficiency is now deemed dependent upon an inadequate supply of insulin. The

reduced power of the tissues to consume sugar seems to parallel the diminishing production of insulin through pancreatic disease. From the excess of sugar in the blood, glycosuria is likely to result. An additional noteworthy fact is that, with the progress of the diabetes, the liver shows a progressive decrease of its power to store glycogen. Just as, in dogs subjected to complete removal of the pancreas, glycogen is absent from the liver, so in the most severe diabetic subjects, glycogen in this organ may be found completely wanting.

That the glycosuria of diabetes is not due to failure of the liver to convert the monosaccharides received from the intestine into glycogen is shown by the behavior of the respiratory quotient, *i.e.*, the ratio of the carbon dioxide eliminated to the oxygen absorbed, in these patients. Whereas normally the respiratory quotient averages 0.8 or 0.82, in severe diabetes, because of the inability to burn carbohydrates, it may drop to about 0.7, indicating the need of a relatively larger amount of oxygen. Ingestion of sugar by the diabetic subject does not generally cause an increase in the respiratory quotient such as is observed in the normal individual (MacLean). There is also evidence of defective fat oxidation in the presence of ketone bodies in the urine.

With lack of insulin as the factor accounting for impaired dextrose consumption in diabetes, the point should be kept in mind that such deficiency of insulin may possibly be the result not only of organic disease of the islands of Langerhans but of extraneous factors influencing the

functional activity of these structures. Among other possibilities, Fitcher recognizes that an influence on the islands is, without question, exerted by the hormones of some of the other endocrin glands through their "accelerator" or inhibitory action. Further investigations will be needed to obtain definite light on these matters.

The absolute and relative amounts of the combined sugar in relation to the free sugar in the blood are doubled in diabetes. Further, when insulin is given, the combined sugar increases as the free sugar declines. Transformation of free into combined sugar may account partly for the hypoglycemia caused by insulin. Biscoe (Clim. med. ital., June, 1925).

There seems no doubt whatever that true diabetes arises from a disturbance in the pancreas resulting in an insufficient supply of insulin to the organism. One might suppose that, like defective sugar oxidation, lack of storage of sugar—to which the writer ascribes glycosuria in elderly individuals,—is also necessarily connected with some pancreatic defect. But if defective storage were always due entirely to an insufficiency of insulin, it is strange that patients showing marked glycosuria and with very little power to store sugar frequently go on for years and years without showing any evidence of defective oxidation. Clinical evidence strongly suggests that, whatever part the pancreas may play, there is another factor present which is very important—apparently the liver. Insulin alone will neither oxidize sugar nor convert it into glycogen. Under certain circumstances the tissue cells may lose, to some extent, their power to form glycogen, even when the normal amount of pancreatic secretion is available. The glycosuria of elderly subjects is very often associated with some changes in the liver. H. MacLean (Lancet, June 12, 1926).

**The Blood in Diabetes.**—Hyperglycemia, the result of deficient glyco-

lysis, is the essential morbid phenomenon in diabetes. The quantity of dextrose contained in the blood ranges in general from 0.25 to 0.5 per cent., *i.e.*, from 0.25 to 0.5 Gm. per 100 c.c. of blood. The usual normal range in the morning before breakfast is from 0.08 to 0.116 per cent.

Where the water content of the blood is reduced because of abnormal urine output, the number of erythrocytes in diabetic blood may exceed the normal range. Generally the leucocyte count is normal, though leucocytosis may occur in diabetic coma. There is constantly a diminution of blood alkalinity, due to the use of bases for the neutralization of acids; normal alkalinity is rapidly restored by insulin. In severe cases, a milky appearance of the serum is not uncommon, owing to the reduction of fat combustion which is known to accompany inability to consume dextrose.

Diabetic blood decolorizes a certain number of coloring substances, *e.g.*, methylene blue, if it is added to the latter in the ratio of 20 mgm. of blood to 1 c.c. of a 1:6000 solution of the coloring agent. This is **Williamson's test**.

**Bremer's reaction** is exhibited in the greenish coloration assumed by dry red corpuscles, fixed upon a glass slide, when they are treated with a mixture of eosin and methylene blue. Red corpuscles from normal blood under the same conditions assume a pink color. I had occasion to observe with Lyonnet—and Bremer admitted it—that this reaction is not peculiar to diabetic blood. We obtained it also with red corpuscles from leukemic blood. The reaction is, therefore, of but limited value.

**The Renal Element in Diabetes.**—Blood under normal conditions contains about 1 Gm. of sugar in 1000 c.c. Normal urine, on the other hand, contains only a few cgm. of it

in the same amount. Thus, the kidneys oppose the elimination of dextrose from the blood when such dextrose is present in it within the normal range of concentration. If the blood sugar rises, however, beyond a certain level, known as the *renal threshold*, the sugar overflows and appears in the urine. This threshold is generally about 0.16 to 0.18 per cent. It varies somewhat, however, in different patients, and may vary in the same patient on different days. In occasional instances, the blood-sugar may be 0.2 per cent. or higher, yet glycosuria be absent. It may be sufficiently high to lead to gangrene or other complications, in the absence of glycosuria.

A number of years ago, I reported the rather extraordinary case of a woman the subject of both Bright's disease and diabetes whose blood, on the last day of her life, contained about 1 per cent. of sugar, and in whom glycosuria was nevertheless exceedingly slight.

Ten cases of diabetes associated with nephritis. In all there was present a marked inability to concentrate urea, as shown by MacLean's urea concentration test. In 8 cases the renal threshold for dextrose was normal. In 1 it was raised slightly; in the tenth case, to a greater extent. Thus, chronic azotemic nephritis does not usually alter the permeability of the kidney for glucose. MacLean's test is of greater value in estimating renal function in diabetes than is blood urea estimation, since the prolonged low diet required in many patients tends to lower the blood urea. E. Wordley (Lancet, Mar. 28, 1925).

Neither the concentrating nor the diluting powers of the kidney are impaired in severe diabetes. There may, however, be some delay or diminution of water excretion. Retention

of sodium chloride may occur, especially if dextrose or urea in large amount is given along with the salt. Apparently the kidneys in diabetics are unable to excrete large quantities of different substances simultaneously. This type of insufficiency may account for the raised renal threshold for dextrose met with in cases of long standing. O. Klein (Wien. Arch. f. inn. Med., June 15, 1925).

**SYMPTOMS.**—With but rare exceptions, the onset of this disease is insidious, and cannot be recognized by the patient. Many cases of diabetes remain entirely unsuspected until the time when some symptom other than the glycosuria attracts the patient's attention. This may be either excessive thirst, polyuria, unusual weakness, or even impotence. More rarely, it is a sudden diminution of the acuity of the vision, or perhaps a complication in the form of furunculosis or balanitis in men, and pruritus vulvæ in women. The daily quantity of urine is increased, except in some rare cases, classed under the head of "*diabetes decipiens*."

**Urinary Symptoms.**—The urine is pale in color; the reaction is sometimes rather strongly acid; the specific gravity, except in some very rare cases, is very perceptibly increased (1025 to 1045 and even 1050 has been met with). The odor is sweet, owing to the presence of glucose, which may amount to, or even exceed, 8 per cent. Generally speaking, the quantity indicated by Fehling's test is a little greater than that registered by the polarimeter. This is due, first, to the fact that the urine contains reducing substances which do not deviate the plane of polarized light, and, second, to the fact that in a number of cases of severe diabetes beta-oxybutyric

acid salts are present in the urine, which deviate it to the left in such a manner that a portion of the deviation to the right, due to the glucose, is masked.

In mild cases of diabetes the true beta-oxybutyric acid is not present in the urine; there may, however, be other substances which deviate polarized light to the left, especially levulose, which has very rarely been met with in diabetes, to the exclusion of the glucose (Zimmer, Külz, Seegen, Neubauer).

Other sugars have sometimes been found; for instance, traces of pentose (Salkowski, Külz), inosite, etc. Külz and Vogel found a mixture of dextrosazone and pentosazone in the urine of 76 out of 80 cases of diabetes. In 64, reaction positive; in remaining 12 cases, doubtful. Pentoses occur, however, in but minute proportion compared to glucose.

Albuminuria exists in diabetes in at least one-third of the cases, but in only a few cases is it symptomatic of Bright's disease.

*Urea.*—Owing to the polyuria, urea is naturally only present in the urine in a very small proportion, but the daily quantity of this substance is often increased. In this respect one may distinguish two classes of diabetics, according to whether the urea is normal or augmented in relation to the patient's body weight. An excessive catabolism of nitrogenous materials is an important morbid factor in diabetes. The relation of urea to the total nitrogen is not noticeably altered, except in grave cases of diabetes, in which the proportion of ammoniacal salts is, as is well known, greatly increased, in order to overcome the acid dyscrasia.

*Uric Acid.*—Very contradictory assertions have been made concerning the excretion of uric acid in diabetics. In reality the *exogenous* uric acid is naturally abundant in those eating a great deal of meat. As for the *endogenous* uric acid, it is a rare occurrence for it to be increased in diabetics; in fact, as a rule it is diminished. In severe cases of the disease an abnormally large amount of the alloxuric bases has at times been detected. This product is often considerably increased, in most instances owing to the meat diet, and, though very infrequently, as a result of the denutrition incident upon the disease.

*Ammonia.*—The increase in the urinary ammonium in a few diabetics was pointed out by Boussingault in the first half of the last century. Its significance was recognized later, when it became known that the production of ammonia in the diabetic subject is often a defensive measure on the part of the economy against acidosis.

*Lactic and Oxalic Acids.*—These acids are sometimes present in excess in diabetic urine, and a few cases have been reported in which the proportion of oxalic acid present was enormous. These are, however, exceptional disturbances of nutrition, constituting in reality a complication of diabetes.

*Chlorides.*—The proportion of chlorides in the urine generally does not present any marked change; there are, however, cases in which a distinct choluria exists (Ascanio Rodriguez).

*Calcium.*—The excretion of calcium salts is considerably increased in the severe forms of diabetes, while in mild forms it is the same or only slightly in excess of that met with in healthy persons.



**Iron.**—An increase in the excretion of iron, probably in relation with augmented hemolysis, has at times been noted.

**Cardiovascular Symptoms.**—Hypertension is rather frequently present in diabetics. A certain proportion of the cases show arteriosclerosis and sometimes present signs of cardiac weakness, *viz.*, a tendency to embryocardia, a considerable degree of acceleration of the pulse when the patient changes from the recumbent to the vertical posture, etc. Such a condition of the circulatory system is truly a complication of the disease, and as such must be taken into account in the prognosis.

In 140 cases, the writer found that in uncomplicated diabetes the blood-pressure is normal or slightly under normal. Nephritis, arteriosclerosis, or aortitis was found in every case showing high pressure. The pressure was not affected by the presence or absence of sugar in the urine. J. Rosenbloom (Jour. of Lab. and Clin. Med., Apr., 1922).

In 90 cases, the author found that diabetic symptoms were frequently preceded by a period of high blood-pressure. Out of 22 cases without glycosuria, the blood glucose was considerably increased in 14, or 63 per cent. Hypertension and renal lesions coexisted in 7 of the 22 cases. Of these 7, 4 showed the greatest increase of blood glucose. Hypertension may thus be regarded as a prediabetic symptom. In established diabetes, if present at all, it occurs in the early period, being seldom present in late diabetes. It is probably due to increased secretion of adrenalin. Marañón (Arch. de cardiología y hematología, Apr., 1922).

There is a special type of diabetes characterized by low blood-pressure. In 2 such cases observed, there were also subnormal temperature and diminished power of reaction to warmth.

Large amounts of sugar and ketone bodies were being excreted. Success in treatment required 4 months, and was not attained until insulin was combined with a nutritious diet and fast days. The patients then gained some 20 kilos. in weight, temperature returned to normal, and the blood-pressure gradually rose. I. St. Lorant (Med. Klin., May 4, 1924).

Contrary to what one might have supposed, the heart is found of small size and the myocardium pale at autopsy in almost one-half of diabetic cases. In one-third, however, I have found the heart enlarged. The hypertrophy of the organ is sometimes dependent upon renal sclerosis or generalized arteriosclerosis; at other times, in relation with a (primary) increase in size of the other organs. As a matter of fact, diabetes does not spare arthritics of massive build and possessing large organs originally any more than it does other individuals.

**Digestive Functions.**—It will easily be realized that the ingestion of an excessive amount of liquids and solids must sometimes lead to disturbances of the gastric digestive function. These disorders seem to depend oftener upon achlorhydria than upon hyperchlorhydria.

In view of the frequency of pancreatic lesions in diabetics, one might suppose *a priori* that the utilization of foodstuffs would often be imperfect in them. But this supposition is not confirmed by the observed facts: The balance of ingested nitrogen and nitrogen excreted in the urine shows that in all but exceptional cases the deficit is slight. Fats, it is true, may not be utilized altogether as well as protein materials. As for the digestion of starchy substances, it is perfectly well carried out.

In a Röntgenological study of the gastro-intestinal tract in 72 diabetics, gall-stones were found in 8 per cent. In 8 more cases there were very suspicious shadows, some of which proved to be gall-stones at subsequent operations. Evidence of gall-bladder region adhesions existed in 26 of the cases. Duodenal stasis was rare. J. T. Case (Jour. Amer. Med. Assoc., Sept. 16, 1916).

**Symptoms Relating to Respiratory Apparatus.**—Diabetics who do not suffer from pulmonary complications show no morbid phenomena in this direction except an increase in the gaseous interchanges in grave cases and a lowering of the respiratory quotient, due, in turn, to the deficient destruction of glucose.

As pointed out by Tirard, however, dyspnea, when urgent, is a grave sign in diabetes. When it develops, one should examine the chest carefully for evidence of tuberculosis or other pulmonary trouble, and also the urine for acetone or diacetic acid, remembering that these may be present even when, or particularly when, the sugar has shown signs of diminishing. When the sugar diminishes and dyspnea is worse, ketone bodies are almost certain to be present.

**General Metabolism.**—The diminution of glycolysis in diabetics is subject to wide individual variations. In a few, it is but slight. It is to be borne in mind, too, that certain sugars are more perfectly utilized than glucose.

Disturbance of fat metabolism in diabetes arises from the fact that for complete combustion of fat, even in normal subjects, a certain amount of carbohydrate must undergo combustion at the same time. It is as if the fat, being less easily oxidized than carbohydrate, required a coincident burning of the latter to maintain its own combustion. When, owing to

deficiency of insulin, the capacity to burn sugar becomes progressively reduced, combustion of the fats is correspondingly imperfect, with resulting accumulation of fatty acids, *i.e.*, diabetic acidosis.

Disturbance of protein metabolism may occur by reason of the fact that it is feasible for the system, when the need exists, of obtaining 58 per cent. of carbohydrate from protein materials. This property of converting protein into carbohydrate, sometimes termed *glyconcogenesis*, is thought to be exercised chiefly through the liver, and comes into play when, in severe diabetes, no other carbohydrate is available for the purposes of the body because of inability to utilize it or because none has been ingested. Thus, when a diabetic fasts and is then fed exclusively on protein, dextrose is derived from the protein in a constant ratio of about 58 per cent. Where a diabetes is total, *i.e.*, no sugar (whether ingested or not) is utilized, and all of the 58 per cent. of the protein is converted into dextrose, it is found that the amount of dextrose appearing in the urine bears a definite relation to the amount of nitrogen excreted, *viz.*, 3.65 to 1, indicating that the dextrose as well as the nitrogen have arisen in a definite way, *i.e.*, through the breaking down of the protein molecules. Such considerations account for the fact that frequently in severe diabetes glycosuria occurs even when the patient is on a starvation diet; under these conditions the body proteins themselves are manifestly being broken down. A similar process goes on in prolonged starvation of a healthy subject; in spite of such starvation, the blood sugar is maintained at a practically

constant level. In most diabetics who have lost their tolerance of carbohydrates, however, the D:N (dextrose-nitrogen) ratio is found to be 2.8:1, the 3.65:1 ratio occurring only in a much smaller number of cases. The former ratio corresponds to a conversion of only 45 per cent., instead of 58 per cent., of the protein into dextrose. In this connection a division of dextrose into two forms, *alpha-dextrose* and *beta-dextrose*, has been found justifiable, the former referring to the dextrose in the 2.8:1 ratio, and the latter to that representing the added 13 per cent. of protein which is converted where the 3.65:1 ratio prevails.

Like the proteins of the food and tissues, the fats may also yield carbohydrate material through conversion where the demand for such material exists. In this connection it is the glycerin, of which the fats yield approximately 10 per cent., which is converted into dextrose. Ringer's investigations indicated that dextrose could be produced by decomposition of the higher fatty acids. According to Von Noorden the amount of dextrose derived from fats is small, but may be greater in diabetics than in normal subjects.

**COMPLICATIONS.**—The complications of diabetes are numerous. It is necessary to distinguish those which are accidents superimposed upon the disease, *e.g.*, phlegmonous processes which are the result of infection, from those complications which form part, as it were, of the diabetic process. Among the latter, acidosis must be placed in the front rank, and will be discussed first.

**Acidosis.**—The healthy average individual eliminates daily about 20

mgm. of acetone through the respiratory tract; a trace of it is also excreted in the urine. If the subject is starved for two or three days, much more acetone will be eliminated. In addition, he will excrete diacetic acid, as shown by means of Gerhardt's test, and even beta-oxybutyric acid. This process of elimination of the acetone bodies occurs owing to the fact that the system is deprived of carbohydrates. Carbohydrate combustion being necessary as a "flame" in which proper fat oxidation may occur, its absence leads to faulty fat combustion with accumulation of intermediate products, *viz.*, the acetone bodies.

Now, in severe diabetes, *with markedly diminished glycolysis*, the system is in reality likewise deprived of carbohydrates, for the reason that the glucose present in the blood and tissues *cannot be utilized*. Diabetic acidosis is thus, in a sense, the necessary result of every diabetes accompanied by a marked decrease of glycolysis. Furthermore, when a diabetic is subjected to a carbohydrate-free diet he is being exposed to the more or less early production of acidosis.

The expression *acidosis* is justified by the fact that there exists an accumulation in the system of organic acids—diacetic (acetoacetic) and beta-oxybutyric acids. It is to be remembered, however, that this form of acidosis is different from that induced by injecting into an animal a solution of a mineral acid. It is a *special* form. Blood containing acetone bodies is more toxic than it would be did it contain an equivalent of an inorganic acid.

The term *acetonemia* has also been used to designate the acidotic com-

plication of diabetes, but, strictly speaking, is applicable only where acetone is alone present. The term *ketone bodies* is often employed as a synonym of acetone bodies, and the condition resulting from accumulation of these substances is referred to as *ketosis*, which term designates the disturbance more specifically than does "acidosis."

That diacetic acid and acetone are derived from beta-oxybutyric acid is a generally accepted fact. But the opposite process may also occur, and diacetic acid yield, by synthesis, oxybutyric acid. In diabetes, the latter is the last of the three ketone bodies to make its appearance.

Detection of acetone and diacetic acid in the urine indicates the presence of acidosis, but their absence is not incompatible with the existence of acidosis, as retention in the system may occur. Beta-oxybutyric acid, which exists in the urine mainly as sodium oxybutyrate, marks a more advanced stage of acidosis. The extent to which this substance may accumulate is evidenced in Magnus-Levy's estimate that from 100 Gm. of fat, 36 Gm. of beta-oxybutyric acid may be formed. Excretion of 5 to 10 Gm. of this acid in twenty-four hours marks a moderate acidosis; excretion of 30 Gm., a severe one.

Acidosis is apt to bring on numerous morbid results, of which the most serious is coma. This will be considered later.

It also gives rise to *lipemia*, a rather common condition which is attributable to failure of proper combustion of the fats in the body. In these cases the blood may contain a large amount of fat,—as much as 100 Gm. or more in 1 liter of blood. The

blood presents the appearance of chocolate to which milk has been added. The very high fat accumulations are, however, exceptional; Boor found the average total blood lipoids in severe diabetes to be 1.41 per cent., as against an average normal of 0.59 per cent. The fat consists to a large extent of olein; but lipoids, lecithin, and especially cholesterol are also present in large proportions. The condition is thus in reality not only a lipemia, but also a *lipoidemia*.

Having thus taken a general view of acidosis, let us now consider the other complications of diabetes.

**Nervous System.**—The most common secondary nervous lesions of diabetes are certain peripheral nervous disturbances, especially those which result in abolition of the knee-jerk. The condition of the knee-jerk was tested repeatedly by Grube<sup>1</sup> in 128 cases of diabetes. It was found normal in 113 and increased in 2. In the latter instances the patients were suffering from a severe form of diabetes. In 4 cases of severe diabetes the knee-jerk was absent or greatly diminished. It was also absent in 9 slight cases. Excluding 3 of these,—because 2 of the patients were tabetic and the third was too obese to admit of satisfactory examination,—there were only 10 patients (7.6 per cent.) in whom the knee-jerk was abolished or greatly reduced.

On the other hand, R. T. Williamson, in an analysis of 50 cases, found both knee-jerks absent in 50 per cent., both present in 38 per cent., and feeble or absent on one side in 12 per cent. In patients under 25 years the knee-jerks were absent in 80 per cent.; under 30 years, in 75 per cent.; over 30 years, in 46 per cent.

The loss of knee-jerks may be ascribed either to changes in the posterior columns of the cord or a peripheral neuritis. It does not seem to have any special prognostic bearing.

The other nervous symptoms are pain and, more rarely, paralysis. The neuralgia of diabetes is very painful and difficult to cure. Worms observed that it is very often symmetrical, and maintained that the pain increases and decreases with the hyperglycemia. Ziemssen was the first to refer this neuralgia to a *neuritis*. There are also lightning pains that somewhat resemble those of tabes.

Diabetic polyneuritis develops as does ordinary polyneuritis of toxic-infectious origin. The prognosis is generally favorable. The toxic products developed in the course of the diabetes act on the nerves like any other toxic products of similar virulence. In a case observed by the writers, ecthyma and gingivitis were the first warning symptoms of the disease. Then sugar was discovered in the urine, and later the polyneuritis developed. Pitres and Marchand (Prog. méd., Sept. 8, 1917).

In diabetes there is frequently an inflammation of the circumflex nerve. The presence of this type of neuritis is demonstrable through the existence of motor disturbances affecting the deltoid muscle. In latent diabetes circumflex neuritis may be of diagnostic assistance. This neuritis is analogous to sciatica in diabetics, and is probably toxic in causation. Sergeant and Kaufmann (Bull. Soc. méd. des hôp. de Paris, May 29, 1925).

According to Lereboullet, attacks of pain even simulating "gastric crises" are sometimes forerunners of diabetic coma.

Vergely reported a case in which there were pains resembling those of *angina pectoris*.

Of the possible *trophic disturbances*, perforating ulcer is the most serious.

The *paralyses* of diabetes present themselves as follows: 1. Limited and incomplete paralysis; this is by far the most prevalent form. 2. Monoplegia. 3. Hemiplegia. 4. Paraplegia. The various forms of diabetic paralysis are sometimes associated, or are combined, with certain unusual phenomena, *e.g.*, facial hemiplegia preceded by facial neuralgia and falling of the upper eyelid, or paresis of the extensors of the left thigh, impeded speech and deviation of the mouth to the left (Charcot), etc. The progress of these paralyses is also somewhat peculiar: they are sometimes migratory and transitory. Some of them are undoubtedly of central origin, but the majority are of peripheral origin, a neuritis forming their anatomical substratum. The peripheral variety is not exempt from this rule, as is proved by the existence, in diabetic paraplegia, of the symptom-complex known as *stephage*, characterized by lowering of the forward part of the foot in walking. This we know is due to paralysis of the foot extensors, and occurs in peripheral neuritis, but not in myelitis.

*Cramps* are another motor disturbance met with in diabetic subjects. These occur principally in the lower extremities, and at night they occasion *insomnia*, which, according to Bernard and Féré, appears to be, in diabetic subjects, the first symptom of disturbance of the cerebral circulation, and may sometimes prove the forerunner of serious symptoms.

*Convulsions* are rare. I have met with a few cases in which they occurred, but, as the autopsies showed, they were not due directly to the

diabetic hyperglycemia, their immediate cause being lesions in the motor areas of the cerebral cortex, brought on through the influence of the diabetic dyscrasia.

*Narcolepsy and Mental Disturbances.*

—More frequently narcolepsy, *i.e.*, a condition of irresistible tendency to sleep, has been noted in obese diabetics. The obesity is the principal cause of this trouble. As for the mental disturbances, they have been carefully studied by Legrand du Saulle. Generally they are characterized especially by melancholia and, in particular, by the fear of being ruined. The chronic vascular lesions in the brain constitute their chief cause, but it also seems certain that the diabetic dyscrasia itself plays a rôle in their production, as they are often observed to disappear or at least to improve when the hyperglycemia and acetonemia are reduced.

Toxic hallucinosis occurred in a case of diabetes observed by the writers. This suggests that in all probability some of the so-called anxious depressions in the literature may have been really of this type. Singer and Clark (*Jour. Nerv. and Mental Dis.*, Dec., 1917).

**Coma.**—Coma is by far the most serious of the nervous complications of diabetes; its termination is almost always in death.

1. *Cardiac coma*: In a few cases, relatively quite rare, the findings at autopsy are limited to lesions of the heart. Frerichs has drawn attention to these cases, and I have reported a typical example: The patient, who was somnolent when brought to the clinic, showed not a trace of acetoneuria, and was relieved exclusively by digitalis.

2. *Coma due to cerebral lesions*:

In another type of cases, not commonly met with either, cerebral hemorrhage or softening is found at the autopsy. In these cases the coma is the result of the cerebral lesions.

3. *Acetonemic coma*: Finally, in another category of cases, which are relatively very numerous, the body is observed at the *post mortem* to give off an odor of acetone; the brain is rather pale and, in addition, there are also *rather often* kidney lesions. Such is the condition revealed in about 95 per cent. of all cases of diabetes that have succumbed in a state of coma. I desire to lay special stress on the fact that renal lesions are rather often met with. While they occur only in a minority of cases, it cannot be asserted that, if uremia plays a part in the production of coma, that part is entirely subsidiary and conditional. I must also add that in a few quite rare cases lipemic thromboses have been found in the cerebral vessels. This complication is, however, of but little importance in view of its infrequency, and it may be definitely asserted that in the vast majority of cases it is the acetonemia alone which is the cause of the coma.

Case of diabetic coma in which marked reduction of intraocular tension caused softness of the eyeball under pressure. Heine holds that a soft eyeball in a patient in coma proves the coma to be diabetic. Riesman (*Jour. Amer. Méd. Assoc.*, Jan. 8, 1916).

Dehydration is common in diabetic coma, though not the cause of the coma, appearing only after the latter is under way. It shows most in the eyeball. In 2 typical cases the specific gravity of the blood was 1064 and 1068, while the reds in 1 case were 8,340,000, while in the other patient copious drinking of

water caused the reds to drop nearly to half their original figure. The pressure in the arteries may be so low as to amount to actual heart failure, with suppression of urine secretion. Hypertonic solutions of sodium bicarbonate should be avoided, since they would dehydrate the blood still more. LeConte and Doric (*Presse méd.*, Apr. 2, 1917).

*Pathogenesis of Diabetic Coma.*—

The acetone bodies—especially beta-oxybutyric acid—possess a rather high degree of toxicity, which is but little inferior to that of lactic acid. According to Desgrez, the intravenous injection into rabbits of beta-oxybutyric acid in the dose of 1.6 grams per kilogram of body weight produces death. Magnus-Lévy found as much as 1 gram of the acid per kilogram of muscle-tissue in diabetics succumbing in coma. The quantity of this acid in the body in cases threatened with coma was estimated by Naunyn at 200 to 300 grams. Others have found about 100 grams of total acid in the form of diacetic acid during recovery from coma. The chief toxic agent in coma, however, is believed to be the beta-oxybutyric acid, which has proven experimentally an active poison of the respiratory center, vaso-motor center, and brain in general, coma resulting from the latter effect.

As previously mentioned, the accumulation of acids is a by-effect of deficiency of dextrose combustion. For a time, the acids are neutralized by sodium and other bases available in the tissues. When these are largely exhausted, recourse is had for neutralization to ammonia, which is produced by the body through conversion of urea in order to supply additional alkali. In incipient coma, accordingly,

as much as 7 or 8 grams of ammonia may be excreted daily, as against 0.5 to 1 gram in normal subjects. Ammonia will neutralize five times as much beta-oxybutyric acid as an equal weight of sodium bicarbonate.

The degree of acidosis required to bring on coma cannot be specifically stated in quantitative chemical terms, since it is subject to rather wide variations, owing to varying conditions of the renal excretory power, carbohydrate and protein storage, and other factors. Onset of coma is favored by excessive carbohydrate restriction, increase of fat in the diet, or starvation from any cause, including vomiting—the latter itself of varying causation. Acute infections and certain general anesthetics are well known to favor acidosis, and constipation, undue fatigue, chemical poisons, alcoholism, and skull fracture are likewise predisposing factors. Elderly subjects, especially after the age of fifty, seem more susceptible to the ketone bodies than children.

The onset of coma is often preceded by an abrupt diminution of the output of urine.

*Symptomatology of Diabetic Coma.*—

The premonitory symptoms comprise: (1) Certain urinary evidences, *viz.*, the presence of an abundance of ketone bodies in the urine, as well as of ammonia; often a diminution of the glycosuria; diminution of the urea nitrogen as compared to the total nitrogen, and copious cylindruria (hyaline and granular). (2) Pulse acceleration. (3) Headache. (4) Anorexia.

Next there appears a symptom which is a close forerunner of coma, *viz.*, altered respiratory rhythm, generally characterized by an abnormal

amplitude of the respiratory movements. In this, the Kussmaul or "air hunger" type of breathing, the disturbance is at first only inspiratory, but later expiration is also seen to be exaggerated. The breathing is loud, although typically free of the stertor observed in cerebral hemorrhage. While deep, it is not generally increased in rate, and is regular. The pulse meanwhile becomes decidedly frequent and of small volume. At first restless, the patient loses his coherency of speech and becomes comatose. A fruity odor of the breath may be noticed. Moderate cyanosis may exist, and the temperature generally falls below normal.

Threatening coma is usually indicated by the occurrence of diacetic acid or beta-oxybutyric acid in the urine, although in a few cases these acids may be continuously excreted without the supervention of coma. Diacetic acid is tested for by *Gerhardt's test*, described in Vol. I, p. 236. In the case of beta-oxybutyric acid, no simple clinical test is available (see Vol. II, p. 267), and this substance is therefore not usually tested for, especially since the presence of diaceturia and acetonuria is sufficient evidence that it exists in the system.

Since the ketone bodies in the urine often do not accurately reflect the degree of acidosis present, and may even be wanting in spite of the existence of marked acidosis, other and more direct tests are sometimes employed, which permit of definitely recognizing acidosis even in its early stages. Such procedures include determination of the alveolar carbon dioxide tension, the alkali tolerance test of Sellards, determination of ammonia excretion in the urine, estimation of the alkali reserve of the blood, and determination of the hydrogen ion concentration of the blood.

Alveolar carbon dioxide tension estimations are conveniently made by Marriott's method (see Vol. II, p. 267). Some allowance in interpreting the results should be made for starvation of any degree that may coexist, since starvation *per se* lowers the

carbon dioxide tension. Vomiting and low caloric diet are possible factors.

The Sellards test is described in Vol. II, p. 268. From a normal maximum alkali tolerance of 10 grams of sodium bicarbonate, the amount of bicarbonate required to alkalize the urine rises progressively with the intensity of acidosis until, in severe acidosis, 200 grams may have to be given before the urine becomes alkaline.

Determination of the ammonia in the urine as an index of diabetic acidosis is readily carried out by the **Ronchese test**: A 10 per cent. solution of sodium carbonate is added, a drop at a time, to the urine until the reaction becomes neutral. Some formaldehyde solution (40 per cent.) is neutralized with a  $\frac{1}{4}$  normal sodium hydrate solution, with phenolphthalein as indicator, until a slight pink tint develops. A mixture of 25 c.c. of the neutral urine and 10 c.c. of the neutral formaldehyde solution is then made and titrated against  $\frac{1}{10}$  normal sodium hydrate solution until a deep pink develops. One c.c. of the soda solution for 100 c.c. of urine corresponds to 0.017 Gm. of ammonia in 1000 c.c. of urine. A daily ammonia excretion of 2 Gm. shows a mild, and 5 Gm. a severe, acidosis.

Estimation of the blood alkali reserve is an even more direct and trustworthy measure of acidosis than the foregoing procedures, but is more time-consuming and less available for clinical purposes. The method of Levy, Marriott and Rowntree is described in Vol. V, p. 369.

The hydrogen ion concentration of the blood, normally 7.35 (oxalated blood), rises in true acidosis, and in severe diabetic coma may reach  $pH = 7.0$ , or even a slightly lower figure. For the methods of hydrogen ion determination, see Vol. V, p. 573.

Coma usually sets in rather abruptly, and when it is once established, no sort of medication, except insulin or, occasionally, an intravenous injection of alkali, is capable of saving the patient. At this time there is usually noted a peculiar lowering of tonicity of the eyeballs, indicating a decrease in the water of the tissues, attributed to excessive aqueous loss through polypnea. Exceptionally, coma-



## DIABETES MELLITUS (LEFINE)

tose diabetics may present convulsions; this occurs most frequently in cases where slight uremia complicates the acetonemia. Death takes place after an interval rarely exceeding thirty-six hours.

**Organs of Special Sense.**—Cataract is the most common symptom; it nearly always develops in both eyes, if not simultaneously, at least with but a short intervening period. It is characteristic of this form of cataract to be relatively soft. Retinitis is next in order, with white exudations along the vessels and in the perimacular region. According to Mauthner, many causes may lead to ocular lesions in this disease. Among them are (1) diminution of water; (2) diminution of resistance of the vessels, due to general weakening of nutrition; (3) the existence of a toxic substance in the blood, produced by abnormal processes; (4) various complications.

From a study of 25 cases in which ocular lesions of various character were found by Hirschberg in association with diabetes, three groups were distinguishable: (1) a characteristic inflammation of the central region of the retina, with small, bright areas, and frequently also small hemorrhages; (2) retinal hemorrhages, with the consequent inflammatory and degenerative changes; (3) rarer varieties of retinitis and degeneration, the relation of which to the constitutional disease remains to be demonstrated.

The retinitis is nearly always accompanied by slight hemorrhages. True optic neuritis is much more rare. According to Saundby, the retinitis of diabetes is distinguished from that of Bright's disease as follows: 1. The patches are irregularly distributed around the center of the retina, not

specially near the macula, and met with on the nasal as well as on the temporal side of the disk. 2. The patches are never arranged in a fan shape. 3. They are never associated with papillitis or diffuse retinitis. 4. The hemorrhages are, as a rule, punctiform, and not striated. 5. Hemorrhages into the vitreous are common.

A retrobulbar neuritis would explain the existence of the central scotoma sometimes met with in diabetes.

Besides the ocular lesions mentioned, Panas, and, after him, Hirschberg, have insisted upon visual disturbances caused by a defect of accommodation.

Out of 7176 eye patients by the last-named observer, 113, or  $1\frac{1}{2}$  per cent., were diabetics. After ten years' existence this disease regularly causes, he states, alterations of the eye structures, particularly the lens and retina. In a third of the cases diabetes then was found associated with some of the following significant changes: (1) uncomplicated paralysis of accommodation in middle life; (2) late myopia occurring between 40 and 60 years, without changes in the lens; (3) retinitis, and (4) quickly developing cataract in young persons in poor health.

There may be functional ocular disturbances with diabetes, either of refraction or visual acuity. There may also be partial paralysis of accommodation, probably toxic in origin, according to Terrien. Myopia is not uncommon; neither is cataract or diminished refraction, or there may be disturbed central or peripheral vision, amblyopia, hemianopsia, etc. Separate muscles may be paralyzed, and diplopia.

Paralysis of the intrinsic muscles

is very rare. Paresis of the abducens sometimes occurs; also a combined paralysis of the oculomotors giving rise to imperfect lateral motion of both eyes. A nuclear origin is evident in these cases.

The frequency and sudden onset of the minor ocular signs of diabetes, such as disturbances of refraction (particularly myopia) and accommodation, may be of diagnostic utility. A congenital predisposition probably exists in these cases. Terrien (*Paris méd.*, Oct. 22, 1921).

Hypermetropia in diabetes appears only after the patient has been placed on an antidiabetic diet. S. Hagen (*Arch. f. Ophth.*, June 14, 1921).

In ophthalmic examinations in 292 diabetics, the writer found eye affections traceable to this disease in 25 per cent., *viz.*, in 82 cases. Out of the latter cases, 52.4 per cent. showed retinal affections; 16 per cent., cataract; 14.6 per cent., transient errors of refraction, and 8.5 per cent., opacity in the vitreous. C. L. Andersen (*Acta ophthalm.*, ii, 250, 1924).

According to Gellé, suppuration of the ear is not rare in diabetics. The progress of acute otitis is the same as that observed in gout: Rapid tumefaction, protrusion, and redness of the tympanum. During the second day severe pain appears, and later there is abundant suppuration from the external meatus.

Inflammation of the mastoid has been observed in diabetes by Urquhart.

According to Potts, there is something almost characteristic in mastoiditis in diabetes in that the mastoid is often attacked without any marked signs of trouble in the tympanum. The destruction of bone takes place more rapidly and extensively than in other cases. On the other hand, when an acute otitis media does precede mastoid inflammation, there will be sometimes an unusually small amount of pain, although the membrane will continue persistently bulging in spite of repeated incision. The lumen

of the canal is apt to be narrowed, due to sagging of the walls, external otitis, or a furuncular condition. The acute inflammatory phenomena are apt to be absent until late, pointing to a low vitality or resisting power, which constitutes an additional indication for early operation. Postoperatively, the granulations have a tendency to become large and flabby. Speed in operating and brief anesthesia are important.

**Cardiovascular System.**—The lesions of the heart have been, until recently, but indifferently studied. The organ undergoes a reduction in size and weight in about one-half the cases. In over one-third of the cases I have found it hypertrophied. Mayer has also observed this, and states that increased cardiac volume, either from hypertrophy or dilatation, is much more frequent in diabetes than one would suppose from the literature, he having found it without other anatomical lesions in 82 out of 380 cases.

These patients are either possessed of a very delicate constitution, with the heart action weak and irregular, or they are obese diabetics, with the face red or cyanosed, who present a strong cardiac impulse and signs of dilatation of the heart, either with or without atrophy. These patients are apt to die suddenly. Such cases should not be confounded with the true diabetic coma; moreover, they differ from the latter by the absence of acetonuria and by the suddenness of death. Very often it is after a voyage or fatigue of some kind that these patients fall into a state of collapse, with cold extremities; small, feeble pulse; a more or less rapid loss of consciousness, and death in a few hours.

Description of a confusing symptom-complex in diabetes, featured by chilliness with cold perspiration, ashy pallor of the face, rapid and soft pulse, cold

hands and feet, muscular weakness, and dilated pupils. In the more pronounced cases the patient may seem to be in severe shock or collapse. As compared to the symptoms of the insulin reaction, the pallor is more marked, and the cold sweating more profuse than the slight moisture which precedes the insulin tremor, though less general and extreme than the later sweating attending an insulin convulsion. Dizziness is common, and there may be various paresthesias, disturbed coordination, and dimness of vision. Faintness may be complained of, though actual loss of consciousness has not been observed. A constant finding, even in mild cases, is low blood-pressure. B. Smith (Cal. and West. Med., Mar., 1925).

Arteriosclerosis is common in diabetics. Ferraro dwells particularly upon generalized endarteritis. According to him, the atrophic and necrotic lesions reported in various organs are due to this endarteritis. That true gangrene (excluding death from acute specific processes, which may occur in any subject and at any age) occurs in diabetic patients unaccompanied by such arterial disease as would of itself produce the gangrene, yet remains to be proved.

Five cases of what the writer regards as an arteriosclerotic coma in diabetes, all ending fatally. While there was a superficial resemblance to true diabetic coma, the breathing was not of the Kussmaul type and acetone was absent or in small amount. Usually there were nervous symptoms such as hemiparesis, positive Babinski, etc. Apparently the brain arteries in diabetes may be affected as are those of the extremities in diabetic gangrene. H. Strauss (Med. Klin., Mar. 13, 1925).

Case of intermittent claudication and fatal cerebral hemorrhage in a diabetic woman of 55 years. There were atheromatous changes in the peripheral arteries. Cholesterol, pres-

ent in excess in the blood, is supposed to have been retained in the inflamed intima of the arteries, promoting hyperplastic changes and vascular occlusion. Letulle, Labbé and Heitz (Arch. des mal. du cœur, May, 1925).

Edema, which is quite common in diabetes, is not always symptomatic of an affection of the heart. It may possibly be due to complication with Bright's disease, or to a venous thrombosis, of which a number of examples have been reported. In most instances, as maintained by Widál, it is caused by a retention of the chlorides,—whence the indication for a chlorine-free diet in these cases.

There is a tendency to sodium chloride retention in diabetics, to which edema may be due. If sodium chloride and glucose are given together, the urine may not contain any chloride at all. O. Klein (Münch. med. Woch., Mar. 27, 1925).

**Pulmonary Apparatus.**—The most frequent complication in this direction is pulmonary tuberculosis. At least one-third of the cases of diabetes treated in the hospitals are admitted on this account. The lesions of diabetic lung trouble are almost always those of tuberculosis. The exceptions met with are cavities following pulmonary gangrene, which, as has been remarked by some clinicians, do not yield the usual fetid odor. There may also occur ulcerations due to a fibrous ulcerative pneumonia.

In the 8 fatal cases out of 14 collected cases of diabetes with tuberculosis, the cause of death was always the tuberculosis. As the latter advances, the glycosuria and acetonuria disappear, carbohydrate tolerance increases, and the need of insulin decreases. Acidosis is generally absent, and none of the cases had diabetic pruritus or furuncles. C. Lundberg (Acta med. scandinav., Apr. 1, 1925).

After phthisis, pneumonia is a serious complication of diabetes.

Pneumonia is rare in diabetes. In 700 cases studied by Bussenius only 7 cases of pneumonia were observed, not counting 1 case of bronchopneumonia and 5 of influenzal pneumonia. In none of these cases did the sugar disappear during the febrile period. It may begin like ordinary pneumonia. I have seen several such cases. The temperature does not differ from that usual in pneumonia, and the urine remains, notwithstanding the fever, at its usual level. There are also cases of rapid pneumonia, of which I have observed several. In the primary congestive period death may ensue in a few hours.

**Digestive Apparatus.**—The gums are usually red and tumefied. Dental alveoloperiostitis exists, as a rule, when the diabetes dates back several years. The teeth soon become loose in the alveoli and fall out, and dental caries is frequently present. In arthritic diabetes pharyngitis is often present, or, at all events, congestion of the pharynx, with the expectoration of bloody mucus.

Garel describes a form of pharyngitis symptomatic of diabetes or albuminuria. There is at first a slight difficulty in deglutition, a sensation of pressure in the throat, and a deposit of mucus which annoys the patient considerably. An examination of the throat shows the pillars of the fauces and the posterior portion of the pharynx to be reddened, the mucous membrane red, swelled, and frequently covered by a layer of glairy mucus. Freudenthal noted a diabetic ulceration of the throat. The ulcers have a tendency to increase in depth and extent, and are extremely painful.

These ulcerations do not present any characteristic appearance or location.

The stomach is dilated in all cases of polyphagic diabetes. In the latter cases the digestion is *apparently* accomplished much more readily than one would suppose in view of the enormous quantity of food taken, but this is often only seemingly the case, as, notwithstanding the absence of symptoms of indigestion, the food is imperfectly dealt with. The hydrochloric acid is often absent in the gastric juice (Rosenstein, Gans, Hönigmann). Sometimes there are lesions of the mucous tract (interstitial gastritis, atrophy of the glands); in other cases no distinct lesions have been observed. Gans and Hönigmann claim to have found hyperacidity in certain cases.

The disturbances of the intestinal digestion are less known, because they are less accessible for investigation.

Among 140 diabetic patients Seegen found the liver enlarged in 28: about 20 per cent. Others have found a greater proportion of enlarged livers, but it is to be borne in mind that examinations made during life do not yield uniformly dependable results. The temporarily congested liver presents a greater volume and consistency than in the cadaver. The differences of opinion concerning the condition of the liver in diabetes are, in a measure, due to this fact.

In certain subjects attacked with severe diabetes, a brownish color of the skin, and especially that of the face, similar to that witnessed in Addison's disease, is observed. But, as stated under Etiology, such lesions are not, as a rule, a complication of diabetes, but occur concomitantly or before this disease.

Hanot and Chauffard published 2 cases of this kind in 1882. Cases were afterward reported by Letulle, Hanot and Schachmann, Brault and Galhard, Barth, and others. Upon section, the liver is found hard and distinctly and uniformly sclerotic, and microscopic examination shows the hepatic cells to be infiltrated with yellowish-brown or black granulations, while at certain points there are large black masses. The sclerotic connective tissue shows by its topographical distribution the existence of bivenous cirrhosis. In the portal spaces obliterative endarteritis is found, with networks of biliary pseudocanaliculi, masses of pigment, and remains of destroyed hepatic cells.

The liver is the seat of predilection for deposits of pigment, but the latter has also been found in the pancreas (Hanot and Chauffard), as well as in slight quantities in the kidney, and even in the heart. Finally, it may occur in the skin itself.

The quantity of iron chemically determined in the pigmented organs is variable: Quinke found in 1 case an enormous quantity of dry matter. The liver was said to contain, in all, 27 grams. Zaleski justly remarks that this pigmentation is not characteristic of iron.

**Urinary System.**—Urinary complications are very common. First there are those due to previous morbid conditions (gout, for instance), and, in particular, there are those which depend upon the diabetic dyscrasia, and which, as is known, are *complex* in the case of gravel diabetes.

The renal lesion most common in diabetes has been reported by Armanni and fully described by Strauss.

It affects exclusively the zona

limitans, where it invades the straight tubules of Henle, which may be either large or slender; sometimes, likewise, some of the collecting tubules (Strauss). As to the localization, there are individual variations; in one instance it was found exclusively in the ascending branch of the loop.

Armanni regarded this lesion as a hyaline metamorphosis. Ehrlich, with the aid of iodized gum, proved that it is really an infiltration of the cells by the glycogenic substance. He regarded it as a constant symptom in diabetes; but this opinion appears to be somewhat exaggerated. At all events, this lesion affords proof of the ease with which the organism synthetically transforms the sugar into glycogen. Ehrlich thought that the sugar so transformed was that contained in the urine. Strauss—basing his opinion upon the fact that the lesion is localized in the zona limitans, in the neighborhood of the capillaries interposed between the uriniferous tubules—is inclined to believe that this sugar comes from the blood of these capillaries. In support of this hypothesis the fact may be advanced that the glycogenic infiltration may take place in other organs besides the kidneys; the brain, for instance (Futterer).

In certain cases of severe diabetes, particularly when death has been caused by coma, Ebstein has seen a peculiar alteration in the epithelium of the convoluted tubules in which circumscribed areas alternate with normal portions. According to Albertoni, this lesion is due to the acetone or to the acids which exist in the blood in severe diabetes.

More recently, and only in cases in which death occurred during coma,

Fichtner has reported a very circumscribed alteration in the cells of the convoluted tubules, which consists of an infiltration of fat at the base of these cells, which is detected by osmic acid. I have also met with this change, to which the attention of pathologists should be directed. In a study by Colcord of 644 post-mortem examinations on subjects who had died of diabetes, the condition of the kidneys was carefully noted in 241. In the remainder they were reported healthy, or only the gross appearances were noted. Of the 241 cases, 68 were noted as hypertrophic; 52 as hyperemic; 94 as the seat of a nephritis; 17 as having fatty degeneration; 7 had epithelial accumulation; 2 had cysts, and 1 multiple abscesses.

Lesions similar to those of Bright's disease rarely occur in the diabetic kidney.

Eight cases of a clinically distinct type of diabetic coma presenting the following features: Blood sugar and blood urea very high; urine usually small in quantity, going on to complete anuria; little or no acetoneuria or diaceturia; some albuminuria; coma often not deep until just before death; air hunger absent or slight; no acetone odor of the breath; prognosis usually fatal, from anuria.

While insulin gives marvellous results in ordinary diabetic coma, it fails in these cases, 7 of the 8 succumbing. With insulin any slight acidosis present was easily abolished, the urine rendered sugar-free, and the blood sugar brought down to normal, yet the patients became worse, secreted less urine, and were finally anuric. There was always some albuminuria, and usually a few casts. Urea in the urine was generally low. There was seldom noticeable thickening of arteries or high blood-pressure. The chief symptoms were vomiting, rest-

lessness, and feeble, quick pulse. The type of respiration varied, sometimes Cheyne-Stokes, but never typical air hunger. Tension of the eyeballs was lowered, as in ordinary coma. Sometimes there was quiet delirium, but never twitchings nor convulsions. Against a uremic causation was that, beyond slight albuminuria, many cases showed no evidence of renal insufficiency, while the symptoms differed from those commonly found in uremia, resembling much more those of so-called urinemia from obstructive suppression of urine. Certain changes found *post mortem* (not specifically described), suggested, however, that the kidneys are an important factor. In the single case which recovered, 2 pints of normal saline solution had been given subcutaneously at the outset, and 4 pints more were introduced during the first 24 hours. A. C. Begg (Lancet, July 11, 1925).

Several authors have dwelt upon the frequency of *cystitis* in diabetic subjects.

A complication which is much more rare is *pneumaturia*, in which the patient toward the end of micturition ejects a jet of gas through the urethra. In a patient observed by Mueller, the gas, which was collected under water, was composed as follows: H, from 44 to 57 per cent.; N, from 33 to 35; CO<sub>2</sub>, from 9 to 19; O, traces; CH<sub>4</sub>, traces. Freshly voided urine contained 1 per cent. of sugar, but sometimes there was no trace of it. No doubt the fermentation of the sugar in these cases is due to the presence of foreign organisms, especially yeast cells or other fungi, in the bladder.

**Skin.**—The cutaneous complications occurring in diabetes are pruritus, eczema, and gangrenous lesions. The pruritus may exist without any appreciable lesions. It affects the genital organs, especially the glans

penis in men. In women it is much more painful, affecting the vulva. It gives rise to an itching, burning sensation, with exacerbations, which may cause insomnia and various nervous symptoms. Sometimes it occurs early and is one of the symptoms first revealing the existence of the disease.

Diabetic eczema is of two varieties: either genital, in which case, like the pruritus, it appears to be due to the local irritation caused by the sugar, or general, when it occurs principally in arthritic subjects. Chronic eczema of the genital organs in women may be pachydermic (Fournier).

The gangrenous dermatoses were carefully studied by Marchal de Calvi, and later by Kaposi.

Furuncle and carbuncle frequently complicate diabetes. The carbuncle presents a somewhat peculiar type, beginning insidiously, and with but little pain; edema is not marked, and the febrile reaction is either slight or does not exist. Very frequently the affection is complicated with a phlegmonous process or with gangrene.

Gangrene may be primary in diabetics, without any previous phlegmon or carbuncle. In this case it is dry or mummified, like senile gangrene. It begins most frequently in the toes, and has been seen to originate simply in a local asphyxia. I have already mentioned the diabetic perforating ulcer.

A form of lichenoid exanthema has been described in diabetes. In a patient seen by Robinson, touching the tumor caused a burning sensation.

Grube observed 9 cases in which psoriasis coexisted with gout, or diabetes, or both; this writer holds that a causal relation between these affections does undoubtedly exist.

Sherwell enumerates the cutaneous disorders observed in diabetes as follows: Generalized xeroderma, which is quite common; eczematous dermatitic manifestations occurring in any region of the skin, especially prone to attack the flexor surfaces, and more especially the genital, anal, and inguinal regions; furuncular and carbuncular manifestations are quite frequent in this condition, and are found generally in the nuchal and gluteal regions; erythematous lesions, some evanescent, others of the graver kind, as erysipelas, are commonly present; gangrene; dermatitis herpetiformis of Duhring; xanthoma diabeticorum; blastomycetic dermatitis.

**Locomotor Apparatus.**—The cartilages may present the lesions upon which Krawkow dwells, which are due to a deposit of glycogen.

Frerichs refers to the lightness of the bones. They have been found to be extremely light in some cases. I have stated above that in serious cases the lime in the urine is relatively increased. Perhaps these anomalies bear less relation to the hyperglycemia than to the acid dyscrasia of the severe form of diabetes, to which we shall now refer.

**Concomitance of Diabetes and Cancer.**—It is not an extremely uncommon occurrence for a cancer to appear in diabetics, and the observation is said to have been made that cancer runs its course more rapidly in these patients than in non-diabetics. A rapid course is not, however, constant in cancer occurring in diabetes.

**Traumatism in Diabetics.**—Wounds heal more slowly than normal in diabetics. Verneuil has compared them in this respect to alcoholics. As for

the converse relationship, *i.e.*, an influence exerted by trauma upon the course of diabetes, it is clearly shown in certain cases.

**Concomitance of Diabetes and Febrile Diseases.**—Febrile affections sometimes favor and at other times tend to prevent glycosuria, according to the nature and virulence of the infection present. A moderate degree of hyperthermia, not of infectious origin, reduces glycosuria by increasing the destruction of glucose. On the other hand, clinical observations show that infection favors the onset of diabetic coma.

Evidence presented indicating that the ill-effects of infection in diabetes are due, not to a disturbance in the ketogenic balance, but to an actual reduction in the amount or proportions of dextrose oxidized. H. B. Richardson and S. Z. Levine (*Jour. of Biol. Chem.*, Mar., 1925).

**Diabetes and Pregnancy.**—Spontaneous abortion is observed to occur rather frequently in diabetic women. At all events, the product of conception comes to term only in two-fifths of the cases. The surviving children, moreover, generally do not enjoy very sound health.

As for the influence exerted by pregnancy on diabetics, it is rather prejudicial than otherwise; but there are exceptions to this. It is difficult, indeed, to formulate any useful generalizations on this point. Each case must be considered individually.

Pregnancy in diabetes does not demand immediate abortion, even if acidosis is present. If pregnant diabetic patients are managed suitably, they will very likely abort less frequently. It cannot yet be accepted that pregnancy aggravates diabetes, and nursing is not contraindicated after confinements. E. P. Joslin

(*Boston Med. and Surg. Jour.*, Dec. 2, 1915).

Among 427 diabetic women in the childbearing period, pregnancy occurred in only 5 per cent. (Von Noorden). The writer's experience confirmed the above ratio. The evidence of sterility does not necessarily parallel the severity of the disease. It is presumed, although without definite pathologic evidence, that diabetes may cause sufficient damage to the ovaries to bring on complete sterility. In 58 cases reported in 1909, there was a mortality of 30 per cent. from diabetic coma during labor or immediately *post partum*, and a 21 per cent. mortality within 2½ months after labor. A number of cases have been reported with slight improvement or no aggravation during pregnancy, but the majority of observers have noted a distinctly detrimental effect.

The intrauterine fetal mortality has been stated to be 50 per cent., often with death of the mother in coma following that of the fetus. A certain number of premature and weak infants, some with hydrocephalus and congenital diabetes, were born of diabetic mothers. Extreme hydramnios has frequently been the indication for premature induction of labor. The moderately severe or severe diabetic should be prevented from incurring the risk of a pregnancy, since, in the writer's experience, the effect of the latter on the damaged diabetic pancreas was not warded off by insulin. It is doubtful whether diabetes mellitus ever develops in pregnancy uncomplicated by toxemia.

Aside from true diabetes, there may be met with in pregnancy (1) renal glycosuria, and (2) a type of diabetes peculiar to pregnancy. The former is due to lowering of the renal threshold, 3 to 5 Gm. of sugar being excreted in 24 hours; does not call for reduction of carbohydrates, and disappears promptly after delivery. The second group is that of cases which develop a hyperglycemia and marked glycosuria, without clinical symptoms of diabetes. In each of 2 such cases ob-



served there was a mild toxemia of pregnancy. The glycosuria disappears *post partum*, and the condition is apparently caused by a transient functional insufficiency of the islet tissue. H. J. Wiener (Amer. Jour. of Obst. and Gyn., June, 1924).

**COURSE.**—While essentially a chronic affection, diabetes may exceptionally occur in an acute form. Authentic cases of this nature are few, because the evolution of the disease may actually have been an incipient one, and have remained unnoticed up to a certain period, when there is a sudden aggravation.

[Loeb reports the case of a chemist who, while in good health, examined his own urine and found it normal. Soon after, he became ill, and experienced violent thirst. At this time the urine contained 8 per cent. of sugar. Death took place in five weeks.]

Death is not invariably the termination of acute diabetes. Several cases of recovery have been reported. Holsti saw, in a man 41 years old, diabetes having a very sudden beginning, judging by the thirst, and which was only subjected to dietetic treatment six weeks later. After three days of abstinence from carbohydrate food the urine, which had contained 8.8 per cent. of sugar, lost all trace of it, and the subsequent use of starchy food did not cause a return of the diabetes. This is, of course, a rare case. More frequently a diabetes having an acute beginning passes into a chronic condition.

A mild form of diabetes has sometimes been described as *intermittent*; it is due in a measure to the influence exerted by a too liberal diet. As soon as a proper diet is instituted the glycosuria disappears. This is not, properly speaking, an intermittent diabetes. Such cases belong rather to

the type of alimentary glycosuria. In a series of 6 cases of recurrent transitory diabetes studied by Dreyfus Brissac, the proportion of sugar was very variable, but usually 30 to 40 Gm. a day. The glycosuria diminished rapidly under a rigid diet. The amount of sugar was generally less in the second and third attacks than in the first, but the attacks lasted longer with each relapse, 1 or 2 Gm. of sugar persisting for weeks or months. As a rule, there was albuminuria, which subsided with the glycosuria. The proportion of uric acid was high. In all cases there was a moderate degree of polyuria. Thirst and hunger were never marked, but emaciation, a sense of physical exhaustion, and depression were prominent symptoms; these recurred with diminished intensity with each attack. Months or years of perfect health sometimes separated the attacks. In 1 case ordinary diabetes supervened. The recurrent transitory variety of diabetes is connected in certain cases with a constitutional arthritism, in others with an acquired arthritic tendency.

Transitory diabetes is not dangerous in itself; it is the expression of a weak constitution or transitory dyscrasia.

True intermittent diabetes is almost independent of the alimentation. Cases of this variety have been reported by Bence-Jones, Baudremont, and others. Saundby reports 1 case. I have myself seen 1 alternating with albuminuria. This form of diabetes is principally met with in arthritic and hysterical subjects. Its appearance depends principally upon nervous causes, mental or otherwise.

**DIAGNOSIS.**—A well-defined diabetes cannot be mistaken by an ex-

perienced physician. The general symptoms, with the glycosuria, establish the diagnosis.

**Diagnosis by Examination of the Urine.** 1. Is there sugar in the urine? If the percentage of sugar found in the urine is considerable, diabetes is probable. If, on the contrary, a minimal quantity is found, there is much room for doubt. Where only a trace of sugar is present, indeed, its presence may be overlooked by the physician; for if it is tested for with Fehling's solution, and there happens to be a rather high percentage of creatinin in the urine, the latter substance, by virtue of its basic nature, will keep in solution the small amount of oxide which should have precipitated. The proof of this as a possible source of error may be had by adding to the urine of a normal individual eating freely of meat a small proportion of glucose (about 2 Gm. to the liter): It will be impossible to recognize the presence of the latter with the copper test, whereas, if the same proportion of the sugar were dissolved in pure water and tested for, its presence and relative amount could be determined with absolute correctness.

A more common mistake, however, is that of believing one finds glucose, when none is present: One not infrequently meets with more or less obese arthritics who present the appearances of diabetes excepting that the amount of urine voided is small. If they are heavy eaters, as is often the case, their urine will contain a large amount of uric acid and other reducing substances, so that an inexperienced examiner will readily believe the reduction observed in the test to

indeed, at times a rather difficult one. Following is the method of attaining it: If the urine contains at least 3 Gm. of sugar to the liter, Nylander's reagent may be used, *viz.*, bismuth subnitrate, 2 per cent., and Rochelle salt, 4 per cent., in 10 per cent. sodium hydroxide; 10 parts of urine are boiled with 1 part of the reagent for two minutes, when, if sugar is present, a blackish discoloration of the fluid makes its appearance. The oxide of bismuth possesses over that of copper the advantage of not being reduced by uric acid, creatinin, etc.; but it is essential that from the urine used all albumin and mucin have previously been removed, since a trace of albuminous matter will blacken the fluid owing to the formation of bismuth sulphide. In case of doubt, the fermentation test should be tried, and especially the urine referred to a chemist, who will determine whether an osazone can be produced from it.

Where no chemist is available, the physician should proceed as follows: In non-albuminous urine deprived of the greater part of its uric acid by preliminary cooling (on ice) and by filtration, sugar may be considered present if the reduction of the cupropotassic fluid takes place in the cold state, as the reducing substances only exert their action at the boiling point. Sugar itself, in the cold state, only causes a reduction at the end of several hours.

If one does not wish to wait, recourse may be had to the following process, which is a modification of that proposed by Worm-Mueller, to determine whether the reduction by heat is partially due to a small quantity of sugar: The exact quantity of 0 decolorize 1 c.c. of

Fehling's solution must first be determined; then a portion of the same urine is fermented. This having been accomplished, it must then be ascertained whether a greater number of cubic centimeters will be required to decolorize the same quantity of Fehling's solution.

Plainly, if a larger quantity is required, a portion of the reducing power must have been due to the presence of a certain amount of sugar. This method is accurate, and its only drawback is that it is not likely to be within the reach of the ordinary practitioner, owing to the precision required in the determinations.

As pointed out by Lintz, the sugar test may fail unless a 24-hour sample is taken. The turbidity of diabetic urine is of practical importance, as it is due to the growth of yeast cells which may cause, by fermentation, complete disappearance of glucose if the examination is not made sufficiently promptly. Many substances other than glucose will reduce the various copper solutions, among the most frequent being conjugated glycuronic acid, alkapton (homogentisic acid), creatinin, uric acid in excess, blood, and lactose. Occasionally, the urine of menstruating women will reduce the copper solution, apparently because of blood in the urine. Blocking of the secretion of the mammary glands may also produce lactose in the urine, the fermentation test revealing the difference. It is easy to eliminate the reducing substances by the Fehling test provided it is properly done, *i.e.*, after boiling the solution and adding the urine drop by drop. Reboiling is not necessary; warming will do. If the reduction is rapid, one may be pretty certain of the presence of glucose; if it is slow and the precipitate yellow, instead of red, the fermentation test will remove the doubt.

The following simpler and clinically available method is quite reliable: *About 4 c.c. of Fehling's solution are placed in a tube and heated to the boiling point; then 1 to 2 c.c.*

*of urine, free of albumin, are made to flow along the side of the inclined tube. [To free urine of albumin, dilute acetic acid is added, the urine boiled, and the resulting precipitate filtered off.] It is well first to heat the urine slightly; or, the inclined tube may be held above a flame for a few moments in order to raise the temperature sufficiently at the plane of contact of the two liquids. After a few moments, if sugar is present, a green ring will be seen to form, which will then rapidly change to yellow, and afterward to red, the latter contrasting decidedly with the blue color of the subjacent liquid. If a red ring is obtained, it is of great value, for the other reducing substances only produce hydrate of copper, which is yellow in color.*

Jastrowitz has advised the examination of the precipitate of oxide of copper under the microscope. It is a fact that none of the reducing substances, uric acid, creatinin, nor the compounds of glycuronic acid, etc., produces a crystalline precipitate. According to Jastrowitz, the copper oxide crystals are tetrahedral and octahedral. These are actually the forms obtained when a watery solution of glucose is made to react upon Fehling's solution, but small spheres may also be produced with urine containing a slight amount of sugar. Thus, when, under the microscope, these spheres predominate, provided they are accompanied by tetrahedral and octahedral crystals, it may be affirmed that sugar is present in the urine.

It is possible partially to get rid of the reducing substances by means of a process described a long time ago by Seegen, and which is to be recommended on account of its simplicity: *The urine is filtered through animal charcoal as many times as is necessary to decolorize it; the charcoal is then washed in distilled water, and the*

two filtered liquids—the urine and distilled water—treated separately with Fehling's solution.

The purpose is as follows:—

The charcoal retains not only the coloring matter and the uric acid, but likewise certain substances, as yet not well known, which prevent the precipitation of the oxide of copper. Therefore, one is better able to investigate for the sugar with the filtered water than with the urine. Furthermore, the charcoal has retained a large portion of the sugar contained in the urine, and gives off into the distilled water a larger portion of the sugar than of the other substances which it had retained. Consequently the reduction of Fehling's solution is much more easily effected by this water than by the urine.

Fehling's solution, provided one knows how to use it, is capable—all statements to the contrary notwithstanding—of alone determining the presence of sugar.

The reducing action of glucose upon the oxide of bismuth in the presence of an alkali has also been resorted to for a long time. This reaction, called that of **Böttger**, which is described in all the treatises on urology, is far from being valueless, especially when employed with the modification indicated by Nylander (see p. 40).

Leaving aside several other tests which have not come into general use because they are not sufficiently accurate, I pass on to the **phenylhydrazin test**, described by Fischer. This test is based upon the property, peculiar to phenylhydrazin, of forming when in combination with glucose a crystalline substance of a

bright-yellow color. Von Jaksch performs this reaction as follows: 10 c.c. of the urine are poured into a tube, 3 pinches of crystalline sodium acetate added, and also 2 pinches of phenylhydrazin hydrochloride. The mixture is placed for a time in a boiling water-bath. After it has cooled, a yellow, crystalline deposit is formed, which, under the microscope, appears to be composed of fine needles, some isolated, others in agglomerations, and some assuming star formations.

It has been said that this reaction is not absolutely characteristic, and that glycuronic acid will also cause needle formations; but Hirschl ascertained that upon leaving the tube one hour in the water bath the glycuronic compounds do not give rise to a crystalline precipitate, and Binet, who made a very complete study of this important reaction, considers it as absolutely reliable with the following slight modifications: 10 c.c. of the urine to be examined, freed of albumin, are cleared with a few drops of lead acetate solution. The liquid is then filtered, and a few drops of acetic acid, 3 pinches of sodium acetate, and 2 of phenylhydrazin hydrochloride are added. The whole is left in the water bath for one hour. The tube is then allowed to cool, and on the following day the urine is examined with a strong magnifying glass. Under these conditions no balls or granular masses are found, but yellow or silvery crystals, characteristic of *phenylglucosazone*. According to Binet, 1:2000 of sugar is thus distinguishable.

I do not believe that the **fermentation test** is superior to the phenylhydrazin test as regards sensitiveness. Brewer's yeast alone, and like-

wise the urine itself, when left undisturbed, gives rise to gas-bubbles. Thus, in order to arrive at certainty as to the presence of the sugar, a control test must be made. Two similar test-tubes are prepared, the suspected urine is placed in one and normal urine in the other, an equal quantity of yeast is added to each, and they are left under like conditions for twenty-four hours.

The **fermentation-specific gravity method** gives results as a *quantitative* test, according to Christian. All that is required is to take the specific gravity of the urine at room temperature, add a small bit of commercial yeast, and put in a warm place, such as an incubator at 37° C., a heated room, near a stove or radiator, etc. Active fermentation soon begins, as evinced by bubbles and currents in the urine. When fermentation is finished, the specimen partially clears and the evolution of gas ceases. A negative test with Fehling's or Nylander's solution proves the end of the process—12 to 18 hours usually sufficing. The specimen is now allowed to return to the room temperature of the previous specific gravity determination, and the specific gravity re-determined. The difference between these two readings, multiplied by 0.23, gives the percentage of fermentable substance expressed in terms of glucose.

The **Benedict test** has come into increasingly wide use, being about ten times more sensitive than the other copper solutions and avoiding various fallacies of Fehling's test; the solution used is not appreciably reduced by uric acid, creatinin, or such preservatives as chloral hydrate, chloroform, and formaldehyde. The test is also advantageous in comparison to Fehling's in requiring but one solution, which, moreover, keeps indefinitely in uncolored and cork-stoppered bottles.

Benedict's solution is made up as follows:—

Copper sulphate (pure crystallized) .....	17.3 Gm.
Sodium or potassium citrate .....	173.0 Gm.
Sodium carbonate (crystallized) .....	200.0 Gm.
Distilled water.....ad	1000.0 c.c.

The carbonate and citrate are dissolved in about 700 c.c. of water with the aid of heat, and filtered, if necessary. The copper salt is dissolved in about 100 c.c. of water and poured slowly and with constant stirring into the first solution. As the last step in the preparation, the mixture is cooled and diluted to 1 liter.

For use, 5 c.c. of the Benedict reagent is placed in a test-tube and 8 drops of the urine added. Heat to boiling for three minutes and allow to cool spontaneously. If glucose is present the entire body of the solution is filled with a precipitate, which may be red, yellow or greenish in tinge, according to whether the amount of sugar is considerable or small. If the amount is small the precipitate forms only on cooling. If no sugar is present the solution remains clear or shows a faint blue turbidity.

A *quantitative* dextrose determination can be made with Benedict's reagent as follows: In a porcelain dish place exactly 25 c.c. of the reagent, add 5 to 8 Gm. of anhydrous sodium carbonate and a little powdered pumice stone, boil vigorously for a short time, and then run in from a burette the urine to be tested—previously diluted 1:10, unless the dextrose content is known to be low. The blue color of the solution diminishes and a white precipitate is formed, whereupon the urine is run in more slowly, the reagent being meanwhile kept boiling, until all of the blue color has disappeared. The amount of urine consumed is read off, and a calculation of the dextrose content made (with allowance for whether the urine was diluted or not) on the basis of the fact that the 25 c.c. of Benedict's reagent is decolorized by exactly 0.05 Gm. of dextrose.

**2. Is the Sugar in the Urine a Manifestation of Diabetes?** The known presence of a sugar in the urine does not alone warrant the diagnosis of diabetes, for the sugar present may not be dextrose (glucose).

*Lactosuria.*—The sugar-containing urine of a woman in whom lactation has just been suddenly brought to a close, and which consequently contains lactose, might be mistaken for a diabetic urine; but the attendant clinical circumstances generally suffice to prevent such an error. Lactose is also distinguished by its failure to ferment with yeast.

*Alimentary Pentosuria.*—I have had occasion to examine a specimen of urine which, judging from its reducing power, appeared to contain several grams of glucose; but it had no rotatory power. The urine was that of a healthy individual who had partaken a few hours before of a large dish of white onions. Its reducing power was due to a pentose (inactive arabinose).

*Constitutional Pentosuria.*—Pentosuria is not invariably of alimentary origin. A few cases of idiopathic pentosuria have been reported. This is a metabolic disturbance which is quite distinct from diabetes, in general not serious, but sometimes associated with nervous phenomena. It is clinically necessary to distinguish it from diabetes, since the customary anti-diabetic diet is injurious to these patients. In a few instances, however, pentosuria occurs in severe cases of true diabetes, the failure to burn sugar having extended to include pentose.

Pentose is distinguished by the fact that it fails to reduce Fehling's solution promptly, a greenish yellow

or muddy orange color appearing abruptly after some delay. It also fails to ferment with yeast, is optically inactive, and shows special absorption bands with the spectroscope.

*Levulosuria.*—The polariscope permits of the recognition, when the occasion presents, of levulosuric diabetes. This variety is extremely rare.

**Non-diabetic Glycosurias.**—The well authenticated presence of glucose in the urine is not sufficient to warrant the assertion that diabetes exists, for various toxic effects or nervous influences, etc., are capable of giving rise to a temporary glycosuria. Where, however, the proportion of glucose exceeds 1 per cent., the condition present is very likely to be diabetes.

The condition known as *renal glycosuria* ("renal diabetes," diabetes in-nocens, renal glycu-esis), is characterized by more or less regular persistence of the glycosuria in spite of fasting, a normal or low blood sugar irrespective of the carbohydrate content of the diet, and the absence of the usual symptoms of diabetes. The blood sugar curve (glucose tolerance test) is particularly useful for the accurate diagnosis of this form of glycosuria; after a dose of 100 grams of glucose by the mouth, the blood sugar should not rise above normal levels and should return to the fasting level within two hours. The glycosuria in these cases may range from a trace to as high as 5 per cent. The condition is ascribed to increased permeability of the kidney cells (lowered renal threshold).

For further data on the renal and other forms of glycosuria, the reader is referred to the article on GLYCOSURIA, Volume V.

**Diagnosis by Examination of the Blood.**—As the reader will have gathered from preceding sections, the presence of glycosuria does not of itself prove that diabetes exists. Glycosuria may be due to a low renal threshold for dextrose; H. J. John has observed glycosuria in non-diabetics with the blood sugar ranging as low as 0.04 per cent. (40 mgm. per 100 c.c. of blood). On the other hand, in diabetics, glycosuria has been known to be absent with blood sugars ranging from 0.12 up to 0.35 per cent.—the renal threshold being often raised in severe diabetes. In a person with somewhat low renal threshold, glycosuria may follow every heavy carbohydrate meal, without such glycosuria signifying the existence of diabetes. The renal threshold may vary at different times in a given individual. In diabetic coma there may be a high glycemia and a low glycosuria.

In view of these considerations, and since a mistaken diagnosis is fraught with unusual risk or unnecessary misery for the patient, blood sugar tests have assumed great importance in the diagnosis. Such tests, furthermore, constitute a distinct advance over uranalysis for the recognition of early or borderline cases, and have raised the possibilities of early diagnosis of diabetes to a level attained in but few other disorders. The aim should, indeed, be to detect diabetes previous to the appearance of clinical symptoms, while the possibilities of efficient treatment or actual cure are at their greatest. Blood sugar studies also prove of great value for the proper regulation of treatment in diabetes mellitus.

The **Epstein modification of the Lewis and Benedict method** affords a relatively simple procedure whereby 0.1 or 0.2 c.c. of blood suffices for a clinically adequate determination of the blood sugar. An apparatus similar to the Sahli hemoglobinometer is used. In a test-tube marked at 1 c.c. and 2.5 c.c. are placed 1 or 2 drops of 2 per cent. sodium fluoride or potassium oxalate solution, followed by exactly 0.2 c.c. of blood from the finger or ear lobe, and distilled water up to 1 c.c. Laking having occurred, a saturated solution of picric acid is added, a few drops at a time, with shaking, up to the 2.5 c.c. mark. After vigorous shaking the mixture is filtered or centrifugated; 1 c.c. of the clear fluid is withdrawn into an ordinary test-tube and carefully boiled until but 2 or 3 drops of it remain. One-half c.c. of 10 per cent. sodium carbonate is then added and the solution again boiled down to 2 or 3 drops. Finally, 3 or 4 drops of distilled water are added, the tube gently warmed, its contents placed in the graduated hemoglobinometer tube, and water added up to the 50 mark. Comparison is made of the resulting color with that of one of 2 standard color tubes (according to the depth of color of the specimen), water being added until the specimen matches the standard. The reading thus obtained, divided by 1000 or by 500 (according to the standard used), yields the percentage of sugar in the patient's blood. Where the sugar content is known beforehand to be high, 0.1 c.c. instead of 0.2 c.c. of blood is used.

**Bang's method** is still simpler, though less precise in its results, than the preceding method. It requires 2 or 3 drops of blood, taken from the lobe of the ear on a piece of blotting paper 16 by 28 mm. The bit of paper is held with forceps, and is not allowed to soak up too much blood. It is then placed in a test-tube. A second test-tube holding 5 c.c. of a mixture of 136 c.c. of saturated solution of potassium chloride, 64 c.c. of water, and 0.15 c.c. of a 25 per cent. solution of hydrochloric acid, is heated, and when it boils is poured carefully over the blood-paper. When entirely cool—not until after  $\frac{1}{2}$  hour—the fluid is poured into a third test-tube, and to it are added 5 drops of the Fehling II reagent and 2 drops of Fehling I. It is then

boiled for  $\frac{1}{2}$  minute and watched for 2 minutes. If no oxide precipitates out in 2 minutes, the proportion of sugar in the blood is below 0.15 per cent., i.e., is within practically normal range. The amount of oxide thrown down is an index of the sugar in the blood.

Following simple procedure described, intended for the use of the general practitioner, for detecting a *decided increase of blood sugar*: (1) Wash out a test-tube  $\frac{1}{4}$  inch in diameter and allow 1 drop of water to remain in it. (2) Place 20 cu. mm. of the patient's blood, obtained with a capillary tube (such as the tube of Gower's hemoglobinometer) from the pricked finger, in the tube and mix it

can thus be demonstrated. In pancreatic diabetes the sugar content was found higher in the blister fluid than in the blood, while the converse was true in mild, temporary glycosuria. Gänsslen (Münch. med. Woch., Aug. 3, 1923).

A fasting blood-sugar estimation alone is not of diagnostic value, but a 3-hour post-prandial estimation gives important results. The patient is instructed to eat a heavy carbohydrate meal and present himself at the office *exactly* 3 hours later. If he is normal, there will be no hyperglycemia, whereas if after the 3 hours the blood sugar is above normal, he is definitely a diabetic, whether or not there be

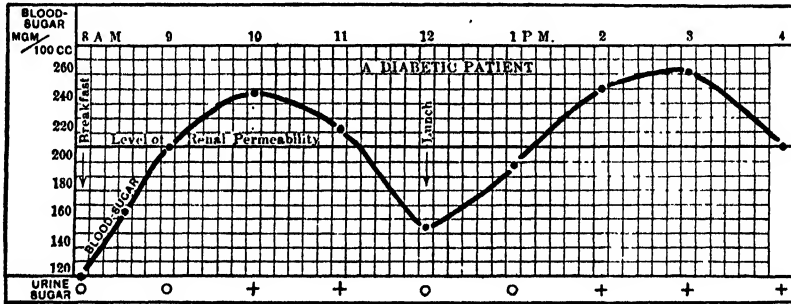


Chart showing curve of blood-sugar after meals in a diabetic. (H. J. JOHN, in *Amer. Jour. Med. Sci.*)

with the drop of water. (3) Add 1 c.c. of 1:6000 aqueous solution of methylene blue. (4) Add 40 cu. mm. of liquor potassæ (B. P.). (5) Mix by placing finger-tip over tube and slowly inverting tube 6 or 8 times. (6) Place tube in a boiling water bath for 4 minutes, keeping tube quite still. If the fluid in tube has lost its blue color, becoming *brownish yellow*, the blood sugar is decidedly increased. A control test with normal blood may be run at the same time. R. T. Williamson (Pract., Sept., 1921).

**Blister test** for the study of sugar accumulation in the tissues: A vesicant plaster measuring 2 by 3 centimeters is placed at night on the outer aspect of the leg or arm, and the fluid withdrawn the next day and tested for sugar. Passage of sugar into the tissues after intravenous injection of it

sugar in the urine. H. J. John (*Amer. Jour. Med. Sci.*, Jan., 1925).

**The Glucose Tolerance Test.**—This procedure is regarded as affording more dependable evidence of diabetes than isolated blood sugar determinations. It will even disclose whether an individual may or may not be apt to develop diabetes, and thus has actual prophylactic value. It eliminates erroneous conclusions from incorrectly performed single blood sugar determinations, and will prevent dismissal as non-diabetic of cases in which the fasting blood sugar has already been reduced to normal and the glycosuria dispelled by treatment elsewhere.



In carrying out the test as employed by H. J. John, a blood specimen is first taken in the morning before food, 100 Gm. of anhydrous glucose then given in 250 to 350 c.c. of water with the added juice of 1 or 2 lemons, ice cold to lessen nausea, and further blood specimens then taken at intervals of  $\frac{1}{2}$ , 1, 2, 3, and 4 hours. The greatest diagnostic importance is attached to the time required for the blood sugar to return to normal after the rise induced by the ingestion of glucose. If this fails to occur within 3 hours, the individual is diabetic.

In normal subjects, according to Jacobson, the blood sugar averages 0.14 per cent. at the  $\frac{1}{2}$  hour period, 0.12 after 1 hour, 0.11 after 2 hours, and 0.09 after 3 hours.

In diabetes the curve is higher, usually reaching at least 0.17 or more (up to 0.60), and, in particular, remains elevated for a longer time. It should be noted, however, that in mild diabetes—that for the detection of which the glucose tolerance test possesses special value—the fasting blood sugar is generally within the normal range.

In the normal blood sugar curve the fasting level must be between 0.08 and 0.12 per cent.; the curve must not rise above 0.2 per cent., and must return to normal within  $1\frac{1}{2}$  or 2 hours in the young or 2 or 3 hours in the aged. It is unaccompanied by glycosuria. While one or two single blood sugar estimations, *e.g.*, 3 hours after a meal, sometimes suffice to establish or exclude diabetes, in mild diabetes the fasting level may be quite normal or raised to only 0.13 or 0.14 per cent., and after food one may find only 0.19 per cent.—figures not of definite significance. In doubtful cases a glucose tolerance test with 50 Gm.

of glucose is required; but otherwise, it should never be performed. If the fasting level has been found to be 0.15 per cent. or the blood sugar after food above 0.22, the fact that the blood sugar rises to 0.3 or 0.4 after 50 Gm. of glucose yields no further valuable information. Such an amount of glucose has a harmful effect, perhaps permanent, in further damaging the patient's pancreas and a bad psychologic effect in leading him to think that sugar cannot be so very bad for him.

The diet before a glucose tolerance test should be a full normal diet because (1) if a mild or potential diabetic has had little carbohydrate for a day or two, the body stores of glucose and glycogen have become depleted and the test may show very little abnormality; (2) starvation or severe carbohydrate restriction may make the curve approximate the diabetic type in a perfectly normal individual and even produce acetone bodies before the test. R. D. Lawrence (Practitioner, Feb., 1927).

**PROGNOSIS.**—Uncomplicated diabetes is a disease which, all else being equal, shortens life, but which, rationally treated, does not implicate an early fatal termination, and can at times even be recovered from. I have had under observation for several years diabetics who might pass as having been cured.

Out of a series of 1187 cases of diabetes the writers were able to trace 1156. Of these, 640 were living and 516 dead. Among them, 62, or 5 per cent., lived 15 or more years, and of these 37 were living and 25 dead. Obesity, which is universal in the long-lived diabetic, existed in 60 of the 62 cases. The average loss of weight when the patient first came for treatment was 41 pounds. Acidosis was demonstrated 21 times, and in 11, or 44 per cent., of the fatal cases the patients succumbed to it. Arteriosclerosis occurred in 36 cases

and was a prominent factor in causing the death of 10 patients. Diabetes had become a minor issue in 50 per cent. of the living patients, and at the time of death was a minor issue in 28 per cent. of those who died. An extremely rigid diet was necessary for only 4 of the patients still living. Of the fatal cases, 20 per cent. outlived the normal expectation of life for their age at the onset of their diabetes, and this was true of 10 per cent. of the living cases. Dietetic treatment was carried out to a considerable degree by 57 of the 62 patients. Of the remaining 5, 3 were among the dead. Hornor and Joslin (Amer. Jour. Med. Sci., Jan., 1918).

Many diabetics have rather good chances of prolonged survival, provided they will consent to have themselves treated. In stout, elderly patients in particular, survival for 10 or more years may be witnessed. Lack of enlightened treatment, however, except in a few cases of transitory traumatic diabetes, inevitably results in aggravation of the disease.

Blood fat analyses are a material aid in the diagnosis and especially in the prognosis. Most long-lived diabetics show blood fats below 1 Gm. per 100 c.c. By blood fats the writer means those substances determined by Bloor's method for so-called "total fat," *viz.*, fatty acids plus total cholesterol but not lecithin. Among 1062 blood samples from 588 patients, the blood fats exceeded the normal maximum (0.67 Gm. per 100 c.c.) in 78 per cent., as against abnormal blood sugar (above 0.11 Gm. per 100 c.c.) in only 72 per cent. In treated cases the blood fat seems, for diagnosis, to be somewhat superior to the blood sugar, showing greater stability. As regards prognosis, the blood fats were found related to the periods of survival as follows: 0.79 Gm., 4 years or more; 0.93 Gm., 2 to 4 years; 1.03 Gm.,  $\frac{1}{4}$  to 2 years; 1.15 Gm., 6 months or less. Severe diabetics develop high blood

fats simultaneously with emaciation, while under treatment a progressive fall of blood fat occurs, even when such treatment is based on the high fat diet. When the fat exceeded 2 Gm., the patient lived less than 2 years in 86 per cent. of cases. H. Gray (Amer. Jour. Med. Sci., July, 1924).

The prognosis of diabetes differs greatly according to the case, the pathogenic factors, the age of the patient, his submissiveness to the regulations imposed by the physician, etc.

The relatively great severity of diabetes in the young cannot be too strongly emphasized. Recovery from diabetes in the child is rare. The use of insulin, however, has greatly reduced the fatalities from coma in these cases. The prognosis seems to be somewhat more unfavorable in women than in men.

There exists a mild type of diabetes in childhood and adolescence. It tends to occur in several members of the same family. The glycosuria is usually moderate, although nervous excitement and other disturbing factors may augment it. The disease is not progressive and may remain stationary or end in apparent recovery. Riesman (Amer. Jour. Med. Sci., Jan., 1916).

The severity of the disease may be judged from the behavior of the glycosuria on a diet free of carbohydrates. If it disappears, the disease belongs to a milder category than if glycosuria persists, the latter condition indicating that the proteins of the body are being utilized as a source of sugar.

Among 425 (pre-insulin) fatal cases, according to Joslin, the actual causes of death were: 16 of cancer; 16 of pulmonary tuberculosis; 62 of cardiorenal and vascular changes, uncomplicated by coma; 36 of in-

fections, pneumonia heading the list; 9 of septic and gangrenous legs; 4 of carbuncles; 2 of acute fulminating appendicitis. Coma was fatal to 273 cases (64.24 per cent.).

Out of 26 autopsied cases of diabetes, of which 17 had received insulin, only 4 died of diabetic coma; 1 of these 4 had not received insulin. Other causes of death were: Gangrene and septicemia, 3; septicemia, 2; perinephric or other abscesses, 4; pneumonia (1 with coma), 2; appendicitis, 2; cardiac conditions, 4; cancer of pancreas, 1; duodenal ulcer, 1; chronic nephritis, 1; phthisis, 1, and inanition, 1. Three of the deaths from coma are regarded as having been preventable, and most of the deaths from septic states could probably have been prevented by proper treatment of minor traumata and furuncles.

The vast majority of cases of diabetes are mild or become so in the course of time. The rarity of death from uncomplicated diabetes in cases of long duration is consistent with the conception of regeneration of the islands of Langerhans. The first 2 years of the disease constitute the danger zone, during which special effort should be made to protect the patient against coma. H. F. Root and S. Warren (Boston Med. and Surg. Jour., Jan. 14, 1926).

To the question, Can diabetics be allowed to marry? I believe it is proper, in general, rather to give a negative answer. If the patient is a young girl, pregnancy cannot be favorable to her, and, as for the product of conception, the chances of its viability are rather poor (in adult diabetic women, however, pregnancy is more often carried to its normal conclusion). If the patient is a young man, the conditions in regard to marriage are not much better, in view of the serious character of diabetes in young subjects. In the case of a middle-aged man, with diabetes of mild degree, marriage is, to be sure, possible; but the virility of a diabetic

cannot be counted on to any great extent.

**TREATMENT.**—Before beginning the treatment of diabetes, the patient should be given as complete an examination as possible, in the course of which he should be closely questioned concerning his habits of life. It is often useful to control his statements by those of persons living with him, points being thus learned which would otherwise have escaped notice. An inquiry into the present condition is then made, as well as into the antecedents and past medical history. The urine examination, next carried out, yields knowledge of the specific gravity and acidity of the urine, of its content of sugar and urea, and of the presence or absence of ketone bodies and albuminuria. In the event that it contains no or very little albumin, *that it does not give a positive Gerhardt test*, that the patient does not present any organic lesions (tuberculosis, etc.), and that there are no metabolic disturbances other than the diabetes—in other words, that the diabetes is uncomplicated, whatever be the percentage of sugar present—the treatment will be a simpler one than in the contrary event.

In such a case there exists, indeed, no fundamental indication other than to reduce the hyperglycemia.

**DIET.**—Since in all diabetics the power of assimilating sugar is more or less diminished, the first desideratum is to limit the ingestion of carbohydrate food. The rule is to forbid it as far as is necessary, and to advise a diet of meat, fish, eggs, and green vegetables, particularly those which contain but little starch.

Where the patient's weight is above normal, marked improvement or even

recovery from the diabetes can be secured by a reduction cure. If the body weight is much below the normal, a more difficult situation may be presented, especially if the glycosuria is considerable and the patient does not bear fats well. In such cases, however, insulin is available for its well-known action in restoring sugar metabolism, and the patient can be made to gain weight.

In all cases the carbohydrates should be reduced, *but under no circumstances should they be completely prohibited*: a certain daily amount, which generally exceeds 80 Gm., is necessary. Otherwise, the patient will be exposed to acidosis.

A simple rule which I have followed is that if the urea excreted does not exceed 0.4 Gm. per kilogram of body weight, the amount of meat need not be reduced; otherwise, I reduce it gradually, meanwhile increasing the fats,—a procedure which does no harm so long as fats are well digested and do not cause ketonuria. (The figure just mentioned is, of course, an arbitrary, empiric one.)

In the mildest cases of diabetes complete or almost complete exclusion of foods yielding much glucose, such as sugar, pastry and bread, together with reduction of fats, will result in cessation of the glycosuria, whereupon carbohydrates can be restored to a total of between 100 to 200 Gm. a day without return of glycosuria. Similar effects may result from a simple reduction of the total intake of food. Such treatment, provided it is persistently continued, sometimes suffices in the obese, middle-aged diabetics or in mild familial cases. In the more severe classes of cases, however, these measures are inadequate.

Reduction of the carbohydrates exerts the advantageous effects not only of lowering the amount of sugar in the body fluids, but also of promoting subsequently a higher degree of tolerance for these substances, the relative degree of functional rest allowing recovery on the part of the organism of a part of its glycolytic activity.

It must be borne in mind, however, that 58 per cent. of the protein ingested and 10 per cent. of the fat can be converted in the body into glucose; consequently, too extensive a substitution of proteins for carbohydrates is not altogether advantageous.

The initial step in the formulation of a diet for a given case is to determine how many calories the patient requires. The simplest estimate for practical purposes is 25 calories per kilogram (2.2 pounds) of body weight (ideal weight for the height, age, and sex) for a patient at rest. For more accurate work, especially in adolescents, the actual weight, as well as the height, age, and sex, are taken into account, and the basal caloric needs calculated by the DuBois or Harris and Benedict formulas (see *BASAL METABOLISM*, Vol. II). Thus, the surface area having been calculated by the DuBois formula from the patient's weight and height, the product is multiplied by the caloric requirement per unit of surface according to the age and sex, as given in the table entitled "Aub-DuBois Standards" (under Basal Metabolism).

Other points to be taken into consideration are that carbohydrates and proteins each yield 4 calories per gram, and fats, 9 calories; that the fats and proteins are ketogenic and the carbohydrates antiketogenic, and

that 1 gram of carbohydrate is required by the body for the proper combustion of 1.5 grams of fats. Every gram of protein will yield 0.46 gram of fatty acids; hence, the ketogenic property of proteins can by no means be disregarded. Fats are calculated as 10 per cent. antiketogenic, since they yield this percentage of glucose. A fundamental requirement is protein, from 0.66 to 1 gram per kilo. of body weight.

The caloric requirement of the patient being known, Woodyatt's formulas are convenient for exact calculation of the grams *per diem* of protein (P), carbohydrate (C), and fat (F) to be given. They involve first, however, the calculation of G (glucose)—the antiketogenic portion of the diet, composed of the total glucose derived from carbohydrate, protein and fat. G is obtained simply by dividing the total caloric requirement (with 10 per cent. added for energy used up in digesting food) by 17. Then:—

$$P = \frac{2 \times \text{weight in kilos.}}{3};$$

$$C = \frac{8G}{10} - \frac{P}{2};$$

$$F = 2C + \frac{P}{2}.$$

Where, as is usually the case, the glycosuria disappears under this diet, slight additions, such as 5 grams of carbohydrate and 10 of fat may be made at intervals of two or three days, if the patient becomes physically more active. In ambulant cases the diet may thus be raised until it affords 1 gram each of protein and carbohydrate and 2.5 grams of fat per kilo. of weight, or even a higher caloric yield if needed—provided no glycosuria appears. If glycosuria

appears with the patient not receiving enough calories to support him in his daily work, insulin may be employed in sufficient dosage to permit of his taking the added amount of caloric values required.

For the formulation of the diabetic diet, after the number of calories of each of the three principal classes of foodstuffs has been decided on, the subjoined table prepared by Joslin is of distinct utility, although especially intended for use in this observer's own system of treatment (see p. 59):—

In the table (p. 52) the safest carbohydrate foods are those in the 5 per cent. division; the 10 per cent. foods come next, and so on. Gluten breads (30 per cent.) and bread (60 per cent.) are not included, being of the highest order of danger. The right-hand section of the table shows the amount of carbohydrate, protein, and fat in 30 Gm. (1 ounce) of the foods upon which diabetic patients may live.

For the mild cases in which both glycosuria and hyperglycemia can be eliminated by restriction of starches alone, Fletcher regards as available the **starch-free diet** formulated by Mosenthal as follows:

**TO BE AVOIDED.**—Sugar in any form. Bread, biscuits and cakes. Toast, rice, crackers, oatmeal, and all other cereals. Sago, tapioca, macaroni, vermicelli, potatoes, carrots, parsnips, beets, corn, beans, peas. All fruits, fresh, preserved, or dried. Jams and jellies (except as below). Pastry, puddings, and ice cream. Sauces and gravies thickened with flour.

**ARTICLES ALLOWED.**—*Soups.*—Clear meat broths, which may contain the vegetables mentioned below.

*Meats.*—All kinds, fresh, smoked or cured, except liver; no flour or bread-crumbs to be used in preparation.

*Sea Foods.*—All kinds of fish, but no oysters, scallops, or clams.

*Eggs.*—In any form, but prepared without milk, flour, or sweetening.



short intervals, preferably daily or on alternate days. Even the least trace of sugar is to be regarded by him as a danger signal, calling for consultation with the physician.

Patients should keep a record of the food taken each day, with the carbohydrate, protein, and fat contained. Slow eating and thorough mastication should be enjoined, partly because the unusual amounts of vegetables taken may be insufficiently chewed and cause diarrhea. Foods of unknown composition should not be eaten.

**Starvation Treatment.**—Guelpa, of Paris, in a paper entitled "Starvation and Purgation in the Relief of Disease," read before the British Medical Association in London, July, 1910, advocated **starvation** as a method of rendering diabetics sugar-free and of lessening their acidosis. J. H. Kellogg (N. Y. Med. Jour., Mar. 25, 1916) holds that to Guelpa belongs the credit for the discovery that a diabetic can abstain from food for several days without danger of increasing acidosis or bringing on coma, and that during fasting the sugar output very rapidly decreases as does also the acidosis. Within two years Kellogg and his colleagues treated 267 diabetics by Guelpa's methods, with very gratifying results.

On the basis of experiments in animals by F. M. Allen (Boston Med. and Surg. Jour., Feb. 18, 1915) which showed that *persistent* diabetes occurred in animals from which nearly all the pancreas—over  $\frac{1}{10}$ —had been removed; and also that in an animal deprived of less pancreatic tissue— $\frac{1}{6}$  perhaps—a diabetes occurred which could be stopped by a carbohydrate-free diet, or checked early by starvation, he concluded that diabetes was not a disease *per se*, but merely the result of deficient pancreatic activity, with a resulting deficient assimilation of certain foods. If, therapeutically, a glycosuria in a partially depancreatized animal is arrested by fasting, and the animal is then placed on a diet that will support life without causing glycosuria, we have the basic principle of

**Allen's method.** The animal may be, and remain, thin under this treatment, but he is strong and lively.

The method is, in brief, as follows: The patient, even though emaciated and showing sugar and acidosis, is put to bed and receives no food whatever, until glycosuria disappears, and then 24 to 48 hours longer. Plain fasting suffices, but, alcohol being a food which does not cause glycosuria, from 50 to 250 c.c. ( $12\frac{1}{2}$  drams to 8 ounces) of whisky or brandy, subdivided into 10- to 20- c.c. ( $2\frac{1}{2}$  to 5 drams) doses, are given in 24 hours. The acidosis then falls rapidly. If coma threatens, large amounts of water and sodium bicarbonate are used and continued a few days.

When the fasting patient shows no sugar during 24 or 48 hours, feeding should be begun, but very slowly and cautiously. The one requirement is that the patient remain free from both glycosuria and acidosis. Any trace of sugar is the signal for a fast day, with or without alcohol. The articles to be considered in the diet are carbohydrates, protein, fat, and bulk. Frequently the first thing given after the fast is carbohydrate: 200 Gm. of vegetables of the 5 and 6 per cent. classes, gradually increased day by day until a trace of glycosuria appears, which is checked by a fast day; thus one learns the carbohydrate tolerance and clears up the last trace of acidosis. After this protein is given, an egg or 2 the first day and nothing else. More protein—eggs or meat—is added day by day until the patient shows glycosuria or reaches a safe protein ration. The purpose is to learn the protein tolerance, and to cover protein loss as quickly as possible. Fat is somewhat less urgently needed, except in very weak and emaciated patients, and can be added gradually. An element of bulk is necessary to give the comfortable feeling of fullness and to prevent constipation. This is provided by green vegetables, which may be fed raw or cooked. When even these cannot be tolerated, they may be boiled through 3 waters, throwing away all the water, thus removing nearly all the starch; the patients generally take these thrice cooked vegetables gladly, without glycosuria. One result of this program is a loss of weight,

but this seems to be beneficial. In subsequent treatment, the patient is welcome to gain weight up to a certain point if he can do so without causing a return of glycosuria or acidosis.

**High Fat Diet.**—Certain considerations underlying the successive tendencies in the dietetic treatment in late years may be summarized thus: A diet of protein and fat alone promotes acidosis. This difficulty is overcome by allowing a little carbohydrate. But sugar is bad for the disorganized pancreas; hyperglycemia must be avoided at any cost (Allen). Furthermore, even the proteins are potential sources of sugar. The proteins could be cut down, but not beyond a certain point, for the body cannot thrive while losing protein. Fats and carbohydrates spare the body proteins. But since the carbohydrates cannot be properly dealt with, it would seem better to use the fats. Hence the view of Newburgh and Marsh, that the correct management of diabetes calls for a high-fat, low-protein and low-carbohydrate diet.

In the Newburgh and Marsh method, the patient is first placed on a diet of about 1000 calories, comprising 70 Gm. of fat, 10 Gm. of protein, and 14 Gm. of carbohydrate. When he has been sugar-free for one to two weeks, it is increased to about 1400 calories, with 140 Gm. of fat, 28 Gm. of protein, and 15 to 20 Gm. of carbohydrate. For small persons this is deemed sufficient for continuous use. In larger persons a second increase may be made to 1800 calories, with 170 Gm. of fat, 30 to 40 Gm. of protein, and 25 to 30 Gm. of carbohydrate. Further additions may be made to suit individual cases.

In 176 cases (reported in 1923) in which such a diet was employed, with the intake sometimes increased to as much as 220 Gm. of fat, 55 Gm. of protein, and 35 Gm. of carbohydrate a day, not only did none of the patients develop acidosis on the high-fat diet, but in those coming in with an acidosis short of coma, this acidosis disappeared on the diet. This method, it is stated, will keep the urine sugar-free and maintain the nitrogen balance, does not induce a hyperlipoidemia, supplies enough energy to permit of earning a livelihood, and is not attended by downward progress in uncomplicated cases.

Newburgh and Marsh dissent from the contention that a fatty acid: glucose ratio of 1.5:1 cannot be exceeded without risk of acidosis.

Varying opinions have been expressed as to the relative merits of the above high-fat diet and the low-fat diet advocated by Allen and Joslin. In this connection it may be noted that while some diabetics will do well on one kind of diet, others will do better on another, without any known reason. Further, the advent of insulin would seem to have reduced the importance of a decision as between the high-fat and low-fat methods, since maximal diet restrictions in the severe cases are no longer a paramount need.

**SPECIAL DIETARY FEATURES IN DIABETES.**—The late advances in diabetic therapeutics have led to emphasis on the totals of carbohydrate, protein and fat taken, rather than on the relative merits and demerits of individual foods. Nevertheless, there remain some features relating to specific articles of diet which are of interest and have some bearing on treatment.

**Bread and Starchy Foods.**—Many diabetics are found to have been consuming starches to excess, and in a considerable percentage of these it is through the ingestion of bread that the largest amount of carbohydrates is brought into the system. One hundred Gm. of bread contain 53 Gm. of carbohydrates (the best quality breads may contain more than 55 Gm.), which, becoming transformed into glucose, will yield a still larger amount of the latter (about 60 Gm.). Thus, a diabetic patient consuming 0.5 kilogram of bread daily can cause, theoretically, to pass into his system more than 260 Gm. of glucose.

The importance of greatly restricting the amount of bread ingested may thus be realized. The diabetic should rarely be permitted to take more than 50 Gm. of bread a day; indeed, it is often prohibited altogether, as also those starchy foods,—macaroni or other pastes, rice, sago,—which, in proportion to their nitrogen content, contain more starch than does bread. The subjoined table, after Boussingault (*Ann. de chim. et de phys.*, 5th series, vol. v.) will give an idea of the relations existing between various foods in this respect.



PERCENTAGE COMPOSITION OF SOME  
STARCHY FOODS.\*

	Proteins.	Fats.	Starch and dextrin.	Water.	Ratio of starch to protein.
Rice .....	7.5	0.5	76.0	14.6	10.0
Potatoes .....	2.8	0.2	23.2	73.0	8.3
Sago .....	9.1	0.6	74.7	13.0	8.2
Vermicelli .....	9.5	0.3	76.4	12.5	8.0
Bread .....	7.0	0.2	55.3	36.5	7.9
French cake ("brioche") .....	10.9	10.9	41.3	17.9	3.7
Gluten preparation .....	21.3	1.0	64.7	12.2	3.0
Dried peas .....	23.8	1.6	55.7	13.5	2.3
Lentils .....	25.0	2.5	55.7	12.5	2.2
White beans .....	26.9	3.0	48.8	15.0	1.8

\*Upon adding together horizontally the figures given in the first four columns it will be observed that the result is not 100. This is because the percentage of the salts has been omitted, and because, in the case of dried peas, lentils, and white beans, the thin covering layer, amounting to from 2 to 3 per cent., is not taken into account.

As for **gluten** preparations, there are available certain biscuits containing more protein than carbohydrate, with a rather high proportion of fat. Some diabetics have done well with these preparations, but their considerable carbohydrate content may be far more advantageously applied in the substitution of larger amounts of residue-yielding vegetables; besides, these preparations entail considerable expense.

**Soy bean**, the seed of *Glycine hispida*, is peculiar in containing little or no starch, though having a large percentage of protein, which may be utilized in the body in place of that of other vegetables and of meat. Some observers have considered it a valuable addition to the dietary.

The **dry vegetables**—peas, lentils, and white beans—referred to in the table presented above, contain, for each gram of carbohydrate, about four times as much of vegetable protein as bread. Theoretically, they should be advantageous in diabetics, since for 1 Gm. of nitrogen there are supplied but 2 Gm. of carbohydrate. It is inevitably difficult, however, for an individual with any appetite to content himself with a single spoonful of peas or lentils. If he takes more than this, he will be ingesting a rather large absolute quantity of starch.

The question of *bulk* in its relationship to the various articles of food is of great importance in diabetes, for if the patient does

not experience the sensation that his stomach is full he will remain quite hungry.

It is preferable to be lenient, therefore, in the matter of watery vegetables, even those looked upon with suspicion by some because of their more or less sweet taste. Squash, for example, may well be allowed—in moderate amounts only, of course. This vegetable, indeed, contains more than 90 per cent. of water and about 6 per cent. of carbohydrate (potato containing 20 per cent.). Protein is itself present in a not inconsiderable amount in squash,—1 part to 6 parts of carbohydrate.

Thus, **green vegetables** constitute very valuable food for diabetics. They are, of course, poor in protein; but they are still more so in carbohydrates, when cooked. Some, *e.g.*, lettuce, contain no more protein than carbohydrate, even when uncooked. Moreover, the green vegetables have the advantage of containing vitamins in abundance.

**Fruits** are prohibited *en bloc* by some. To be deprived of them is, however, a hardship to many patients. Besides, such a restriction hardly seems justifiable when it is recalled that almost all fruits, even those with a distinctly sweet taste, contain hardly any more carbohydrates than the vegetables which diabetics are allowed. Weight for weight, fruits contain six to twelve times less carbohydrate material than wheat bread (Kraus). About 200 Gm. of *peeled* oranges are required to equal the amount of sugar occurring in 20 Gm. of bread.

In apricots the proportion of carbohydrates is but little greater. In the peach it is even slightly less. This fruit, therefore, permits of satisfying the whims of diabetics. Even in consuming 100 Gm., they ingest only a small quantity of sugar.

It must not be forgotten, moreover, that among the various saccharine substances, estimated all together, and termed "sugar," all is not necessarily harmful to the diabetic. Thus, pentoses, even when not utilized by the body, can in most instances pass through the system without any prejudicial effect; they increase the *glycuria*, but not the *glycosuria*. Other sugars are utilized, if the amount taken is not too great, *e.g.*, levulose.

A few diabetics tolerate lactose fairly well; but it is especially in **milk** itself that

it is availed of. Now, milk is a complex food product, and lactose is not the only principle in milk which might augment the glycosuria. In addition to 50 Gm. of lactose to the liter, milk contains about an equal proportion of casein, which can yield sugar. Maurel, of Toulouse, brought about recovery in diabetics with the "milk cure"; in these cases the milk acted through suppression of excessive alimentation and stimulation. In most cases the tolerance for milk is low. Although when on a strict *régime* the patient has no glycosuria, the latter appears after ingestion of a half-liter of milk. The use of lactose-free milk has therefore been advised. Wright has suggested the following method of preparation: To the milk are added 3 or 4 parts of water acidulated with acetic acid; the casein and fat are thus precipitated. The milk is then filtered through cheesecloth, and the precipitate washed and redissolved in a saline solution containing in suitable proportion the salts of the blood serum. Patients, however, generally find this artificial milk unpalatable. It may be sweetened with saccharin. Williamson merely dilutes cream with water. Cream contains almost 4 per cent. of lactose, but, since only a rather small amount of it is mixed with a liter of water, the patient ingests, on the whole, but little sugar. Unfortunately the taste of this mixture is hardly satisfying. Kefir, which contains no lactose, but a little alcohol and lactic acid, is generally much more readily accepted.

Von Noorden has advised **oatmeal** in diabetes: It is given, however, in admixture with a large amount of fat, so that the term "oatmeal cure" is not strictly correct. According to Blum, oatmeal does not act in a specific manner, and that which lends effectiveness to the treatment is the interpolation of "vegetable days" (*i.e.*, days of insufficient alimentation) and the prohibition of meat. The action of oatmeal appears to be complex. The intestinal flora is said to take part in it, apparently by causing, when meat is wholly excluded from the diet, partial fermentation and oxidation of sugar in the intestine. Von Noorden noticed that the oatmeal cure did not succeed when the patient ate meat. Hence the fact that only vegetable proteins are given with it. As a matter of fact, not-

withstanding the great notoriety this "cure" enjoyed, it has succeeded only exceptionally.

The nature of the **proteins** taken is not without importance. In certain diabetics meat—especially raw meat—produces much sugar, and casein, even more than an equal weight of egg protein. Vegetable protein is the variety that yields the least sugar. As a general rule, the proteins which produce the most sugar are those which are most rapidly absorbed.

In diabetics *without acetonuria*, free use—not abuse, however,—of **fats** finds few contraindications other than obesity and the condition of the digestive tract.

Fresh cream, fresh butter, animal fats, and cocoa are generally well borne, even in considerable amount. There are diabetics who will readily take olive oil, and even some who, having no distaste for cod-liver oil, are benefited by taking it.

**Intarvin**, introduced by M. Kahn, consists chiefly of glyceryl margarate, small amounts of other fats, and 12 per cent. of liquid petrolatum. The margaric acid is exceptional among fats in containing an odd number of carbon atoms, in consequence of which its oxidation produces no oxybutyric acid and little or no glucose, even in diabetics. It nourishes and strengthens the patients without producing ketosis, yields 8.1 calories per gram, and has generally been given in amounts of 100 Gm. a day. Its taste being slightly rancid, it may advantageously be given melted in hot coffee, before meals. According to Lyon, Robson and White, addition of intarvin to a stabilized diet causes a trace of sugar to appear in the urine, although the substance possesses advantages over other fats.

As for **alcohol**, there is general agreement as to the necessity for forbidding to diabetics sweet liqueurs; champagne, which may contain over 12 per cent. of sugar; vermouth, which may contain 11 per cent., etc. Beer must also be forbidden, especially certain varieties that contain 5 per cent. of carbohydrates. Cider is also deemed harmful. But ethyl alcohol in moderate amount, diluted with water, or in the form of a good quality of wine, may be taken, except where there are contraindications arising from the condition of the liver or alimentary tract. Alcohol sup-

plies, for each gram ingested, about 7 calories; at times it favors the digestive functions, and it does not increase the glycosuria.

**Condiments with a Sweet Flavor.**—**Saccharin** (*Glusidum*, U. S. P.) is used by diabetics because of its sweet taste. It is employed in the preparation of certain food products intended for their consumption, notably chocolate. Although its harmful properties have been exaggerated, there is no doubt that it is capable of causing dyspepsia. Its use may be tolerated, but should not be recommended. **Levulose**, according to S. Solis-Cohen, does not increase the excretion of sugar. **Lactose** and **inulin** are also used to replace sugar. **Hediosite**, which has a pleasant, sweet taste, has been recommended in doses of 10 to 30 Gm. (2½ drams to 1 ounce) a day. **Glycerin** has been used instead of saccharin as a sweetening agent, and has been shown by McCann and Hannon and by Thomas, Jr., to have antiketogenic value.

**INSULIN.**—This product, which has in some respects revolutionized the treatment of diabetes mellitus, is obtained from the islands of Langerhans in the pancreas, and was first prepared through the labors of Banting and Best, in the laboratory of J. J. R. MacLeod, in Toronto, by ligation of the pancreatic duct in animals, thus causing the acinous portion of the gland to atrophy, followed by the making of a saline extract of the residue. Later, the active component having been found soluble in alcohol, and the otherwise destructive external pancreatic ferments being inactivated by the same agent, the way was opened for a more expeditious method of preparation, directly from normal adult ox pancreas. The term “insulin” is derived from the latin *insula*, an island, referring to the islands of Langerhans, certain cells of which, the  $\beta$  cells, have been found degenerated or destroyed in

diabetes and are regarded as supplying an internal secretion essential to the prevention of diabetic glycosuria. The term *iletin* (insulin-Lilly) refers to the first commercial brand of insulin placed on the market; this preparation is supplied in 5 or 10 c.c. vials (U-10, U-20, U-40, or U-80) containing 10, 20, 40, or 80 clinical “units” in each c.c. (1 clinical unit =  $\frac{1}{3}$  the amount of insulin required to lower the percentage of sugar in the blood of a normal rabbit weighing 2 kg. and starved for 24 hours, to 0.045 per cent. within 3 hours). According to Abel and Geiling, the activity of insulin is due to its content of sulphur in an unstable form. They have concentrated it to a point where 1 mgm. is equivalent to 80 units.

An insulin-like principle termed *glucokinin* has also been isolated from plants and invertebrate animals rich in glycogen. It promotes the burning of sugar when injected in rabbits and dogs.

**Action of Insulin.**—Insulin has been found in animals to yield the following effects: It lowers the blood sugar in normal rabbits; it may prevent the hyperglycemia due to piqure, asphyxia, epinephrin and ether; it increases the sugar consumption by the isolated mammalian heart; it causes glycogen to be deposited in the liver of diabetic animals fed with sugar; it raises the respiratory quotient in such animals; it affects the migration of fat in diabetic animals, and causes the acetone bodies to disappear from their urine. (Insulin Committee, Univ. of Toronto.)

Clinically, insulin is not to be considered as a complete cure for diabetes. In conjunction with carefully regulated dietetic treatment, how-

ever, it produces remarkable results in overcoming glycosuria, reducing blood sugar to normal levels, removing ketones from the urine and blood, relieving the symptoms, and increasing body weight and strength in advanced cases. It is most strikingly a specific in diabetic coma, and the alkali reserve and alveolar carbon dioxide of patients in acidosis and coma are restored to normal.

The action of insulin in causing a burning up (or, according to some, a withdrawal to the tissue cells) of the excess of sugar in the blood is so prompt and powerful that an overdose easily leads to an opposite condition—hypoglycemia—with symptoms so pronounced that the term “insulin shock” has been applied. High dosage in animals produces tetanic convulsions, coma, and death. In man, hunger, weakness, or fatigue may be first complained of. Olmsted and Kahn describe a *prodromal stage* of headache, giddiness, restlessness and numbness of the extremities; a *second stage* of chilliness or sense of warmth, sweating and paleness, and a *stage of hypoglycemia* (with blood sugar from 0.06 to 0.04 per cent.), characterized by a shaking chill without fever, muscular tremors and hypothermia. Unconsciousness supervenes as the blood sugar reaches 0.03 per cent. (Joslin), and death is a possibility. An effective and rapidly acting antidote is available, however, in the administration of carbohydrate food. From 1 to 3 teaspoonfuls of glucose or the juice of an orange may be given for the purpose, and the desired result may be further hastened by previous intramuscular injection of 1 c.c. (16 minims) of 1:1000 adrenalin solution. If

the patient, after the adrenalin, is not able within a few minutes to swallow some glucose, the latter may be administered subcutaneously or intravenously.

**Indications and Manner of Use of Insulin.**—In a large proportion of cases—75 per cent., according to the Insulin Committee's estimate—diabetes may be controlled by dietetic treatment, without insulin. The question suggests itself, however: If insulin completely eliminates glycosuria and hyperglycemia, why not disregard all dietetic restrictions and confine the treatment to the administration of enough insulin to make good the deficiency in activity of the islands of Langerhans in the patient concerned? The answer to this is that insulin is an agent capable of *rapidly* producing harmful effects, and that if a dose of insulin overbalances the carbohydrate present in the blood at the time, the symptoms above referred to will promptly appear. Correct insulin dosage requires precise knowledge and adjustment of the diet, and the higher the dosage the greater the risk of dangerous symptoms attending an unadjusted or irregularly followed diet. The necessity of administering insulin with the syringe rather than by mouth—the oral route hindering its activity—is another factor which militates against the substitution of insulin for dietetic treatment.

On the other hand, insulin used in conjunction with diet in the more severe cases is of great value in that it removes the necessity of restricting the patient's food intake and mode of life to conform to the degree of remaining function of the islands of Langerhans. He need no longer

be condemned to a condition of "invalidism and mere vegetative existence, terminating either in coma or death from inanition" (N. B. Foster). On the first and second days of insulin treatment, as noted by Banting, Campbell and Fletcher, the urine becomes sugar-free, and on the second or third day, ketone-free. Strength increases before the end of the first week. Hunger is replaced by appetite, thirst is lessened, and edema disappears in about 10 days. Increase of weight can be promoted by supplying food in excess of the caloric requirements and with it an increased amount of insulin.

Prevailing views as to the correct treatment of diabetes favor a preliminary study of the ability of the case to respond to dietetic treatment alone, insulin being added where such treatment proves insufficient to eliminate glycosuria and maintain for the patient a satisfactory standard of living and working capacity. Joslin (Jour. Amer. Med. Assoc., June 2, 1923) has prepared the subjoined diet table for use in connection with the insulin treatment. It includes preliminary test diets calculated to bring out the patient's ability to respond to dietetic treatment alone:

The four Test Diets (T. D. 1, 2, 3 and 4) are given on successive days until the urine is sugar-free. This generally occurs on Test Diet 3 or 4. One then skips to that maintenance diet which has about the same quantity of carbohydrate as the last test diet used, and advances each day. If glycosuria returns, for example, on the carbohydrate and protein and fat for the sixth day ( $C_6 + PF_6$ ) and the patient is not receiving enough calories, one lowers the carbohydrate to  $C_5$  or  $C_4$  and advances the protein and fat to  $PF_7$  or  $PF_8$  or more as needed, or even adds extra fat in the form of cream or butter. The 5 per cent. vegetables re-

ferred to in the table are those given in the first 2 columns in the table on p. 52, the first series containing 1 to 3 per cent. of carbohydrates, and the second, 3 to 5 per cent. In calculating the carbohydrate of diets, the average carbohydrate of the whole group of 5 per cent. vegetables is reckoned as 3 per cent. In using insulin blood sugar tests are desirable, but usually Benedict tests of each specimen of urine are substituted. By testing before and after meals the patient learns whether the relation between carbohydrate and insulin should be changed. If glycosuria is present although the carbohydrate in the diet is below 30 Gm., insulin is increased. After a few weeks the urine testing can generally be reduced to that portion of the 24-hour urine which is voided at home.

Insulin, when used, is injected oftenest in the arm, next the thigh, and last, the abdomen or buttock,  $\frac{1}{4}$  to  $1\frac{1}{4}$  hours (usually  $\frac{1}{2}$  hour) before meals, according to the estimated rapidity of absorption of carbohydrate from the stomach and of insulin from subcutaneous tissues. The daily dose is calculated on the basis of the fact that 1 unit of insulin is capable of burning 2 Gm. of sugar. With the patient's tolerance for carbohydrates determined, the number of insulin units needed is calculated by dividing the grams of glucose appearing in the urine on the existing diet by 2. If the sugar excreted is below 20 Gm., the drug may be given before breakfast in a single daily dose of 10 units or less, according to the number of grams of sugar. Where the sugar exceeds 20 Gm., two or three doses, before meals, are indicated. Few cases require more than 50 units a day. A "tuberculin" type syringe—1 or  $1\frac{1}{2}$  c.c.—is very convenient for insulin administration. The syringe and needle should be boiled once daily, and washed with alcohol and boiled water previous to other injections.

## INSULIN DIABETIC DIETS (JOSLIN)

DIET		TOTAL DIET				CARBOHYDRATE (C)						PROTEIN AND FAT (PF)				
		Carbohydrate	Protein	Fat	Calories	5½ Vegetables	Orange	Oatmeal	Shredded Wheat	Unceda	Potato	Egg	Cream 20% fat	Bacon	Butter	Meat
Test...	T. D. 1	181	46	44	1304	300	300		3	4	240	3	120			
	T. D. 2	101	35	43	931	300	300		1	2	120	2	120			
	T. D. 3	66	24	37	693	300	300		1	2	120	2	120			
	T. D. 4	34	15	30	466	300	200					1	120			
Maintenance	C1 + PF1	14	15	30	386	300						1	120			
	C2 + PF2	22	19	37	497	300	100					2	60		15	
	C3 + PF3	32	24	37	557	600	100					2	60		15	
	C4 + PF4	42	29	52	752	600	200					2	60	30	15	
	C5 + PF5	52	32	66	930	600	200	15				2	60	30	30	
	C6 + PF6	64	44	83	1179	600	200	30				2	120	30	30	30
	C7 + PF7	74	52	88	1296	600	300	30				2	120	30	30	60
	C8 + PF8	84	61	94	1426	600	300	30		2		2	120	30	30	90
	C9 + PF9	98	65	106	1606	600	300	30	1	2		2	180	30	30	90
	C10 + PF10	109	66	119	1771	600	300	30	1	2		2	180	30	45	90
	C11 + PF11	135	80	135	2075	600	300	30	1	2	120	2	240	30	45	120
	C12 + PF12	139	84	135	2187	600	300	30	1	2	240	2	240	30	45	120

Presenting an outline for the practitioner of the principles underlying the use of insulin, Banting (Proc. Internat. Conf. on Health Prob., 1924) alluded to a vicious circle whereby the excessive hunger resulting from failure to burn sugar throws an increased strain on the insulin-producing mechanism, rapid emaciation resulting.

The basal food requirement of the body is about 25 calories per kilo. of weight per day. Of protein,  $\frac{2}{3}$  Gm. per kilo. per day is required, and the remaining calories must be supplied by carbohydrate and fat in a ratio that will prevent the production of ketone bodies. The simplest method for determining the amounts of the 3 basal foodstuffs to give is that of Hipwell, in which the percentages of calories to be derived from protein, carbohydrate and fat are put down as 12, 13 and 75, respectively. By dividing the protein and carbohydrate calories by 4, and the fat calories by 9, the respective grams of each are obtained. Thus, if a patient weighs 64 kilos., the minimum caloric requirement is  $64 \times 25 = 1600$  calories. The diet prescribed, then, is:

$$\text{Fat: } \frac{75\% \text{ of } 1600}{9} = 133 \text{ Gm.}$$

$$\text{Carbohydrate: } \frac{13\% \text{ of } 1600}{4} = 52 \text{ Gm.}$$

$$\text{Protein: } \frac{12\% \text{ of } 1600}{4} = 48 \text{ Gm.}$$

With these 3 amounts determined, the patient's diet is then compiled by the use of calorie food tables.

Patients should be thoroughly instructed, taught urinalysis, the calculation and preparation of a diabetic diet, and how to administer their own insulin and calculate its dose. They should be warned of the symptoms and treatment of overdosage. It is impracticable for the physician to treat and teach the patient unless he is in a hospital. Blood-sugar estimations are desirable, but not absolutely imperative if the urinary sugar is closely followed.

In the initial examination of the patient, attention should be given to the finding of a possible *focus of infection*. The tonsils, teeth, sinuses, chest and digestive system are examined clinically as well as by X-ray, and special consideration is given to biliary tract infection, constipation and chronic appendicitis. Such a focus, if found, should be suitably treated, as it may lower and unbalance carbohydrate tolerance.

The patient is placed on the diet of basal caloric value for 3 or 4 days, or until the urine is sugar-free. The sugar excreted is estimated daily, and this, subtracted from the available carbohydrate ingested, gives approximately the utilization. The available carbohydrate includes 56 per cent. of the protein, 10 per cent. of the fat and all of the carbohydrate in the diet. If the patient be-

comes sugar-free and "blood-sugar-normal" on the basal requirement diet, the caloric intake is gradually increased until sugar appears in the urine. The tolerance is thus ascertained. If a patient remains sugar-free and has a normal blood-sugar on a diet containing 700 calories above his basal requirement, the case is considered *not sufficiently severe for insulin*; otherwise, **insulin** treatment is commenced. The initial dose should not be more than 5 units twice a day. This can be gradually increased until the patient becomes sugar-free, the diet being kept constant. Roughly, each unit of insulin causes  $1\frac{1}{2}$  to  $2\frac{1}{2}$  Gm. of carbohydrate to be utilized. The amount of utilization per unit is least in severe cases with high blood-sugar and during infection. The insulin is best given 20 to 30 minutes before the morning and evening meals, *e.g.*, 15 units (hypodermically) before breakfast and 10 before dinner, the larger morning dose being intended to take care of the noon meal also. When the insulin dose and diet are balanced so that the blood-sugar is normal, they are concurrently increased until the required amount of food is reached.

An excessive dose of insulin causes a marked *hypoglycemic reaction* beginning in  $1\frac{1}{2}$  to 6 hours (average 3 to 4) and featured by an unaccountable anxiety, restlessness, often sweating, a great desire for food, and soon after, clonic tremor, impaired co-ordination, pallor, rise of pulse rate to 100 or 120, dilated pupils, faintness, and even aphasia, collapse, unconsciousness, convulsions and death. Ingestion of **orange juice** (4 to 8 ounces—120 to 240 c.c.), **glucose** or **candy** relieves these symptoms in 5 to 10 minutes. If coma or convulsions have occurred, **adrenalin**, 10 to 15 minims (0.6 to 1 c.c.), usually restores consciousness in 3 minutes, whereupon glucose should be given by mouth.

By careful adjustment of the diet and dose of insulin, all diabetics may be kept sugar-free. There is abundant evidence of regeneration of the islet cells when the strain thrown on them by a high blood-sugar is relieved. Increase in tolerance is evidenced by decreasing insulin dosage, and some moderately severe cases become able to dispense with the insulin. The proper burning of carbohydrates under in-

sulin allows of complete oxidation of the fats, and acidosis disappears.

Only about  $\frac{1}{3}$  of the cases ordinarily seen need **insulin**. Undernourished diabetics, young diabetics, diabetics with a surgical complication and diabetics with acidosis or an acute infection usually need insulin, while elderly and obese diabetics do not. There is a tendency for too many diabetics to be sent to hospitals for education and treatment. Patients can now learn readily how to calculate diets, measure and prepare them, test the urine for sugar, and administer insulin. Selected cases can be intensively treated with insulin, so that a satisfactory therapeutic result can be accomplished in a few hours. Attempts should be made to shorten the hospital treatment for diabetics. R. Fitz (Boston Med. and Surg. Jour., Mar. 19, 1925).

The large majority of diabetic *children* cannot be successfully treated without **insulin**. With it, 31 of 35 cases treated for a year or more showed marked and progressive improvement of tolerance, the dose being reduced in spite of the increasing body weight. After a precautionary determination of the blood sugar, 3 to 5 units may be given safely at the start, and the dose then adjusted as the effect suggests. Patients receiving less than 10 units daily are given a single dose 15 to 20 minutes before breakfast; 10 to 30 units, in 2 doses before the breakfast and evening meal, spaced 12 hours apart, and with the noon meal somewhat lighter; over 30 units, 3 doses before meals. The usual symptoms of hypoglycemic reaction in children are abnormal epigastric sensations, hunger or actual pain, and crying spells or sudden irritability. Therapeutic results are obtained quickest by beginning with a starvation diet for a day, using insulin if the blood sugar is excessively high. In the mild cases it is equally satisfactory to give the basal requirements, alone or with insulin until sugar-free. The final diet is determined by the child's nutritional needs,

and not by his tolerance. Enough insulin is given to render the extra food utilizable and keep the blood sugar normal. The caloric requirement is determined by allowing the calories as estimated by Holt for the expected weight of the child, or by giving twice the expected basal requirement. Two to 3 Gm. of protein are allowed per kilo. of expected weight, depending on the age. The remaining calories are distributed between fat and carbohydrate in the 1.5:1 ratio. Adequate rest is essential. All foci of infection should be removed early. G. L. Boyd (*Amer. Jour. Dis. of Childr.*, Mar., 1925).

Modifications of insulin dosage and often of diet are unavoidable to counterbalance changes caused by activity or minor illnesses, if the patient is to steer a level course between hyper- and hypoglycemia. The most useful time to estimate the blood sugar is at its lowest point, about 4 hours after the largest daily dose of insulin, *viz.*, usually about noon or just before the midday meal. The level at this time should be about 0.1 per cent.; if it is above, 2 or 3 more units of insulin should be given; if below 0.08, a few units less. R. D. Lawrence (*Practitioner*, Feb., 1927).

### OTHER MEDICINAL AGENTS.

—**Antipyrin** has sometimes been used in diabetes. My researches, however, showed that it tends to counteract the destruction of sugar. Its use cannot be long continued. **Sodium salicylate** has also been of service; its action is similar to that of antipyrin, but it does not likewise diminish the polyuria. **Quinine** acts similarly, and has the advantage of being tonic.

**Opium** reduces both the polyuria and the glycosuria, and may fulfill certain indications. It is in no sense, however, a curative remedy. Slowing of the absorption of sugar from the gastrointestinal tract is thought to account at least partly for its effects.

Having used **codeine sulphate** for a number of years, and then **morphine** in gradually increasing doses, Bassler concluded that the dried extract of **opium** gives the best results, started in  $\frac{1}{2}$  grain (0.032 Gm.) doses, three times a day, and gradually increased until 4 to 6 grains (0.26 to 0.39 Gm.) daily are taken. In some, **arsenic** acts better than opium. **Fowler's solution**, commencing with 3 minims (0.18 c.c.) and gradually increasing up to 10 (0.6 c.c.), three times daily, is most convenient and answers all purposes.

**Extract of oxgall** and **pancreatic extract** often prove effectual, according to L. N. Boston. When using them, it is well to direct that they be placed in pills coated with keratin and a second coating of salol.

Two cases of insulin-resistant diabetes, in which death in coma occurred after reduction of acetoneuria and glycosuria by insulin. To remove the remaining traces of sugar in relatively resistant cases the writer recommends that tincture of **opium** be used as an auxiliary to the insulin. Arneth (*Klin. Woch.*, June 11, 1925).

Striking results claimed for raw **fresh pancreas** in diabetes, the urine becoming sugar-free, the blood sugar declining, and the ketone bodies disappearing from the urine. The gland must be quite fresh and eaten at once, preferably minced and in a salad. One patient seemed to do better on raw gland than on insulin. T. J. Hollins (*Brit. Med. Jour.*, Mar. 14, 1925).

Patient on a constant diet, given raw fresh pancreas, but without diminution of glycosuria. Next day this glycosuria was reduced to traces by a very moderate dose of insulin. Duly controlled experiments have not shown any utility of raw fresh pancreas. Carrasco-Formiguera (*Brit. Med. Jour.*, Sept. 26, 1925).

Case in which raw pancreas checked glycosuria, whereas insulin had failed to do so. The urine remained sugar-free as long as pancreas was given. Neve (*Brit. Med. Jour.*, Mar. 13, 1926).

In a few cases **belladonna**—or **atropine**,—combined or not with opium, has seemed useful.



Forchheimer deemed **atropine methylbromide**,  $\frac{1}{15}$  grain (0.009 Gm.) *t. i. d.*, gradually increased to  $\frac{1}{15}$  grain (0.034 Gm.), or **atropine sulphate**,  $\frac{1}{150}$  grain (0.0004 Gm.), gradually increased to  $\frac{1}{20}$  grain (0.0032 Gm.), well adapted to milder cases. The glycosuria is often diminished and carbohydrate tolerance increased. The tincture of belladonna, however, seemed best tolerated.

**Alkalies** are useful in nearly all diabetics and for a prolonged period. They are known to favor oxidative processes, and possibly they may contribute to the fixation of glycogen in the liver, that is, to what I have termed "euзоamyliа." In certain cases, however, they increase glycosuria; these are generally diabetics in a poor state of nutrition.

A number of cases were greatly improved, according to Labbé and Perochon, by inhalations of **ozone** in daily 15-minute *séances*. Possibly the oxygen in a nascent condition enhanced the consumption of sugar in the tissues.

Natural **sulphur water** found useful in 9 cases. Insulin likewise contains a considerable amount of sulphur. Diabetes is regarded by the writer as a disease due to deficiency of sulphur for pancreatic function. Marchisio (Gazz. d. osp. e d. clin., June 8, 1924).

Favorable results claimed for parenteral **protein therapy** in diabetes. Small doses are injected on alternate days and subsequently every 4th day, with slight progressive increase of the amount. G. Singer (Wien. klin. Woch., Jan. 1, 1926).

**Jambul**, a plant of the order Myrtaceæ, possesses only a very feeble action in diabetes.

**Hepatic opotherapy** has been recommended by Gilbert and Carnot in cases where the functional activity of the liver-cell is distinctly diminished. Sometimes it has given good results in these cases.

Case of *renal glycosuria* in a girl under observation from the age of 6 to 18. The glycosuria sometimes rose to 4.4 per cent., was little affected by diet, but showed slight orthostatic variation, and orthostatic albuminuria co-existed. The general health remained good. Under intravenous injections of **calcium chloride** the glucose was reduced to 0.25 Gm. and the albumin to 0.04 Gm. in 24 hours. Labbé (Ann. de méd., Apr., 1922).

**PHYSICAL AGENCIES.**—**Physical exercise**, recommended long ago by Trousseau and Bouchardat, may be given first rank among the physical therapeutic measures. Unless insulin is given, however, it cannot be advised to all patients, and must even be prohibited in the stage of impaired nutrition, for fatigue increases the latter. Thus, over strenuous physical exercise acts in the same manner as mental strain, worry, etc.

In a diabetic ingesting a moderate proportion of carbohydrate and receiving an adequate supply of insulin, the effect of **exercise** is beneficial, rapidly lowering the blood glucose to a normal level and diminishing the production of ketones, and so rendering tissue metabolism more complete. As a result of exercise the blood sugar tends to fall to between 0.07 and 0.10 per cent., but does not become lowered further. No hypoglycemic reactions have occurred on exercise even if the initial blood sugar was as low as 0.07 per cent. In a moderately severe case with insufficient insulin, however, exercise produces little or no effect on blood glucose and ketosis is increased. K. S. Hetzel (Brit. Med. Jour., Jan. 17, 1925).

**Climate.**—The value in diabetics of a winter sojourn in a warm climate does not appear to have been sufficiently appreciated. The results of rather exact observations seem to have shown that their glycosuria, all

other conditions being equal, is less if they stay in a warm climate. This may be due both to the fact that the activity of glycolysis is augmented and that the system is not excited through the influence of the cold to an increase in carbohydrate metabolism.

**TREATMENT OF DIABETIC ACIDOSIS AND COMA.**—The prevention of acidosis and coma calls for frequent and systematic tests of the urine for acetone and diacetic acid. As soon as these bodies are found—by means of tests previously described—the principal indication is to bring about their disappearance, and with it the immediate threat of serious complications.

To dispel ketosis, where the diet previously imposed has been severe, the patient should, in the first place, be allowed to ingest daily some 50 to 100 Gm. of carbohydrates. In other words, **partial restoration of carbohydrates** is in order. The glycosuria will be increased thereby, but when the acetonuria shall have ceased the glycosuria may be restrained by again reducing the carbohydrates. As carbohydrate material in such cases it is advantageous to give **levulose**, either in the form of **orange juice** or as the pure sugar. The reason for preferring this particular compound is that it is the most readily oxidized among all the sugars. Another agent sometimes employed is dilute **oatmeal gruel**.

As for the fats and proteins in the diet, opinions differ as to which of these should be the more markedly restricted. In certain cases, apparently, an actual excess of fats or even of proteins may have been responsible for the acidosis rather than insufficiency of carbohydrate allowance.

At all events, a justifiable aim is to endeavor to balance the ketogenic and antiketogenic components of the diet, in the manner previously outlined in this article. In this connection it should be borne in mind that in stout diabetics, there is a greater possibility of the production of ketone bodies from the fats stored in the body, while in thin diabetics this possibility is much reduced, a more liberal allowance of fats than in the stout patients being therefore warranted.

To accelerate excretion of the ketone bodies, the intake of **water** should be increased to the largest amounts that the patients can conveniently ingest, or, if the giving of sufficient fluid by the mouth proves impracticable, physiologic **salt solution** may be given by **proctoclysis**, **hypodermoclysis**, or **intravenously**.

The giving of **alkalies**, such as **sodium bicarbonate**, while less highly regarded than formerly, may do some good through a diuretic action; by forming salts with the fatty acids and thus rendering them more soluble, and by sparing the alkaline reserve of the body. The dosage is from 1 to 3 ounces a day (30 to 90 Gm.), in divided amounts and well diluted, preferably between meals. A serviceable guide as to dosage is the reaction of the urine, which, from marked acidity, should be changed to neutrality or slight alkalinity. If possible, determinations of the alkali reserve of the plasma should be made and the drug administered until this reserve has been restored. Neutralization of the ketone acids does not, of course, insure that their production will cease.

Where acetonemia has been of long standing, it is occasionally found im-

possible to arrest its progress, even by rational diet and other measures, unless **insulin** is also used.

The *prophylaxis of coma* may be secured by instructing the patients, whenever ill from any cause, to **go to bed, keep warm, take a glass of hot water, tea, broth, orange juice, or oatmeal gruel** every hour, empty the bowels with an **enema**, and call a physician, who, if he finds acidosis, will probably administer **insulin, digitalis, and caffeine**, and may **wash out the stomach**. Patients omitting insulin through lack of supply must go to bed and restrict the diet one-third. E. P. Joslin (Jour. Amer. Med. Assoc., June 2, 1923).

**Diabetic Coma.**—Vastly improved results in diabetic coma have been afforded by **insulin**, which should be administered at once in these cases. Even in advanced coma, unless it is complicated by other morbid conditions or the patient is actually moribund, recovery nearly always occurs under repeated intravenous injections of insulin in conjunction with enough glucose to obviate reduction of the blood sugar to a dangerously low level. By inducing combustion of **glucose**, insulin likewise enhances that of the fatty acids, thereby overcoming the symptoms.

After an initial dose of 40 units of insulin subcutaneously, 20 more units every 3 or 4 hours are likely to be needed, or, in severe cases, even 40 units. Proper adjustment of dosage calls for frequent tests of the urinary sugar and the ferric chloride test for diacetic acid, or better, where facilities are at hand, determinations of the blood sugar and carbon dioxide-combining power of the blood plasma. For the practitioner to whom the latter tests are not available, the necessary procedure is to collect urine

every hour or two, the bladder being emptied each time—by catheter, if need be,—and to carry out tests for sugar and acetone. Insulin can be continued as long as sugar is appearing in the urine. If, in spite of disappearance of sugar, acidosis is still indicated by the urine tests or clinical condition, injections of 10 or 20 units of insulin may be continued, to be followed immediately and in the succeeding 3 hours by injection of an equal number (10 or 20) of grams of **glucose**, given either by mouth, or subcutaneously in 3 to 5 per cent. solutions, or intravenously in 5 to 50 per cent. solutions of pure, sterile glucose.

Generally, the injections of insulin at short intervals will be required for three or four successive doses. When the ferric chloride reaction has become faint, the intervals are lengthened to 6 or 8 hours. **Fruit juices** may advantageously be given as soon as consciousness returns. The administration of at least 40 units of insulin a day for two or three days is advisable, after which a maintenance diet may be instituted. Care should be taken immediately after recovery from the coma so to adjust insulin dosage as to escape both a recurrence of the coma and, on the other hand, unconsciousness from hypoglycemia due to excess of insulin. These perils are best avoided either by frequent determinations of the blood sugar or, if these are not feasible, by testing all portions of urine passed.

Auxiliary measures in the treatment of coma include the forcing of **fluids**, 5 ounces (150 c.c.) being given every hour; moving of the bowels, preferably by **enemas**; **external heat** to the body and extremities; absolute

rest, and the use of circulatory stimulants such as **digitalis** and **caffeine** when the occasion arises. To dilute the fatty acids and facilitate their elimination, as well as to provide carbohydrate for promoting their proper combustion, ingestion at short intervals of **orange juice** or a well **diluted gruel** of oatmeal or other cereal is of great advantage. Where the liquids taken by the mouth are not sufficient to subserve these purposes, rectal, hypodermic, or intravenous administration of physiologic **salt solution** or a 5 per cent. solution of **glucose** (dextrose) is of value.

The use of **sodium bicarbonate** in developed coma is well known to be less serviceable than it is when begun earlier. Joslin has discarded it, but some others deem it worthy of trial. If, as many believe, the comatose state is due mainly to the toxic action of beta-oxybutyric acid on the brain, mere neutralization of this acid to form a sodium salt cannot necessarily be held to terminate its toxic action. Indeed, experimental evidence arguing against such a favorable effect from neutralization seems to be available in the conclusion reached by Ehrmann, Esser and Loewy, that injection of neutral oxybutyric salts induces coma. Previous to coma, sodium bicarbonate may be given by mouth, as already mentioned, although intravenous injection of the drug affords better chances of preventing the onset of coma. A sudden change in the osmotic equilibrium such as will result from an intravenous injection of alkali may well be attended with a much closer contact of the alkali with the toxic substances within the brain cells than would a slow introduction of alkali by the intestinal route. In-

deed, this osmotic change throughout the economy is often followed by the elimination of a large quantity of ketone bodies—as though a flushing of the tissues with fluid had taken place.

When coma already exists, an intravenous injection of alkali has, by itself, but little chance of proving efficient. At most, one may succeed by its administration in bringing the patient back to consciousness for a short time. The toxic bodies inducing coma simultaneously cause lesions of the nerve-cells in the brain which soon become irremediable.

Following are a few practical details concerning the intravenous administration of alkali: A solution of 18 Gm. ( $4\frac{1}{2}$  drams) of sodium bicarbonate to the liter (quart) of ordinary water is prepared. This is boiled, then filtered. A vein is next exposed at the bend of the elbow, a sterile glass cannula fastened into it with thread, and the solution introduced at  $36^{\circ}$  C. ( $96.8^{\circ}$  F.) under low pressure and very slowly. I have run in as much as 1800 c.c. ( $3\frac{3}{4}$  pints) of the solution. In this event the introduction of the fluid occupies a period of one hour and a half. Meanwhile, the pulse is watched and the heart auscultated; if gallop rhythm should be heard, this would indicate that the right heart was being overburdened. Entrance of the fluid should then be temporarily stopped.

The intravenous injection is followed by a reaction (afebrile), which is, in general, favorable. I have observed cessation, through the effect of this reaction (previous to the discovery of insulin), of progressive acetonemia which alkalies administered by the mouth had not succeeded in overcoming.

Olmsted and Kahn recommend in diabetic coma that if, after 6 hours—60 units of **insulin** having been given in 3 intravenous injections—

the blood alkali has not risen markedly, **sodium bicarbonate** should be given intravenously in doses of 25 to 50 Gm. ( $\frac{5}{8}$  to  $1\frac{3}{8}$  ounces).

When a patient is admitted to hospital in diabetic coma, blood and urinary sugar and acetone estimations are to be made as soon as possible, the urine being obtained by catheterization, if necessary. Meanwhile, the large bowel is evacuated with **copious enemas**. If sugar and acetone are present in large amounts in the urine, 30 to 50 units of **insulin** are at once given subcutaneously. The blood and urinary sugar should be frequently estimated, because of the danger of hypoglycemia. To prevent the latter, 30 to 50 Gm. (1 to  $1\frac{3}{8}$  ounces) of **glucose** in 10 per cent. solution may be given intravenously or by rectum. If the patient is profoundly comatose the insulin may be given intravenously with the glucose. He usually regains consciousness in 3 to 6 hours. From this time on fluids and glucose may be given by mouth, if retained. The patient should be urged to take at least 200 c.c. ( $6\frac{7}{8}$  ounces) of **fluid** per hour. Next day, **protein** may be given every 4 hours, *e.g.*, the white of 1 egg in 200 c.c. of **orange juice**. In 2 or 3 days, when ketone bodies have disappeared from the urine, **fat** is cautiously added, and the patient is slowly raised to a basal requirement diet. During coma, the patient is **kept warm**, and **purgation** and repeated enemas given. Much **fluid** is administered—intravenously, subcutaneously or by rectum. Signs of circulatory failure are met by appropriate stimulation. Striking results follow such treatment, especially if begun early in coma. Cases complicated by severe infection, gangrene, pneumonia or intestinal intoxication may, however, recover from acidosis and coma but succumb to the complication. Banting (Proc. Internat. Conf. on Health Probl., 1924).

The comatose patient should have a warm bed with **blankets** in place of sheets, and at least 4 **hot-water bags**

should be kept on hand. A specimen of urine is to be tested for sugar and diacetic acid every hour until recovery. If a self-retaining catheter is left in the bladder, **methenamine**, 10 grains (0.6 Gm.), should be given every 4 hours for 3 doses. **Gastric lavage** should be performed to prevent or relieve gastric dilatation. **Liquids** by mouth must be given **hot** and not exceeding 100 c.c. ( $3\frac{1}{8}$  ounces) an hour. Liquids by rectum—**salt solution**, **black coffee**, or **tap water**—may be given every 2 hours for 2 doses and thereafter every 4 hours. If the patient is dry, one should unhesitatingly give **salt solution** **subpectorally** or, in the presence of pulmonary râles, **under the skin of the thighs**. If the intravenous route is preferred, give very slowly 250 to 500 c.c. and no more until at least 1 hour has elapsed. One c.c. (16 minims) of **adrenalin** from a sterile ampoule may be added to the salt solution when the systolic pressure is below 90. **Caffeine sodio-benzoate** is injected subcutaneously, 5 grains (0.3 Gm.) every hour for 4 doses, and thereafter as indicated.

The **diet** should not contain over 50 Gm. of carbohydrate, 25 Gm. of protein, and 25 Gm. of fat in the first 24 hours, unless warranted by unusual improvement. This is represented by oatmeal, 30 Gm. dry weight, equivalent to 500 Gm. of thin gruel; orange juice, 250 Gm. (juice of 2 small oranges); the whites of 5 eggs, and medium cream, 120 c.c. Broths, coffee, tea, or cocoa shells may be utilized as vehicles for the above.

The **insulin** dosage depends upon an estimation of the probable number of hours the patient can live without insulin. If the expectation of life is 24 hours, inject 20 units hourly until there is clinical improvement and sugar in the urine or blood is approaching normal; if the expectation is 12 hours, inject 40 units in the same manner, changing to 20 units as the condition warrants; if the expectation is only 6 hours, inject 40 units every  $\frac{1}{2}$  hour until improve-

ment occurs. Further, no patient should come up to within 2 hours of death from coma without having received at least 150 units in the preceding hour. Joslin (Boston Med. and Surg. Jour., Oct. 15, 1925).

**SURGICAL OPERATIONS IN DIABETICS.**—In mild diabetes the indications for surgical intervention are not essentially different from those appertaining to non-diabetics. It should be borne in mind, however, that the advent of infection in a diabetic causes a prompt and pronounced increase in the severity of the diabetes, with diminished carbohydrate tolerance and a corresponding secondary increase in the severity of the infection. Both the hyperglycemia and acidosis are promoted, furthermore, by general anesthesia, with the result that the majority of operated cases of severe infection in diabetics, in the pre-insulin era, succumbed. An efficient preventive of such accidents is at hand, however, in **insulin**. If one can start with insulin before operation one may be reasonably sure that the patient will not die of diabetes. In some of these cases, when the infection has subsided the diabetes proves to be of a mild grade, and the patient can be kept comfortable without continuing insulin.

In emergency operative work in diabetics not previously prepared for surgery, intravenous injection of 500 to 1000 c.c. of a 5 per cent. solution of pure **glucose**, with 1 unit of **insulin** added for every gram of the sugar administered, will greatly reduce the risk. **Fluids** should be given freely. Preferable where possible, however, is postponement of the operation until, by **diet** and, if necessary, **insulin**, the blood sugar has been re-

stored approximately to normal and an adequate reserve of glycogen in the tissues established. Intravenous injection of glucose and insulin is, further, advisable at the time of operation.

Excluding premature degenerative changes, especially arteriosclerosis and myocarditis, diabetes, under careful control, does not materially increase operative mortality. In the preparation for operation, hyperglycemia, dehydration, ketosis, acidosis, undernutrition, and depletion of the carbohydrate stores all require consideration. In emergency operations, maximum amounts of **insulin** should be given during the time available before operation, to reduce the blood sugar. Dehydration, manifest in thirst and later in dry tongue and skin and the soft eye, calls for as much as 3 or 4 liters of **fluid** for 2 or 3 days. Any well developed ketone intoxication should be actively treated by increase of carbohydrate and insulin. In severe ketosis, usually with infection, as much as 50 units of insulin, with enough glucose to control hypoglycemia, may be needed. Acidosis generally clears up with the ketosis under insulin; if it is marked, **alkali** may be given, under control of the CO<sub>2</sub>-combining power of the blood. Under insulin, any **diet** can be prescribed which may be needed to strengthen the debilitated patient. Thirty grams of carbohydrate may be given over and above the usual amount calculated to prevent ketosis. Twenty to 40 Gm. of glucose or other carbohydrate and 15 units of insulin should be given 2 or 3 hours before the operation. After operation ketosis may develop very rapidly and means must be taken to reestablish adequate carbohydrate utilization. F. N. G. Starr and A. G. Fletcher (Surg., Gyn. and Obst., Feb., 1926).

#### **TREATMENT OF GANGRENE.**

—Dry gangrene in diabetes may be treated like the senile form of gan-

grene, *i.e.*, by expectancy and **antiseptic dressings**. As for moist, rapidly spreading gangrene, the only rational plan of treatment is to **amputate** early through the healthy tissues. **Nitrous oxide-oxygen anesthesia** should be used instead of ether or chloroform.

If the patient is too weak to bear amputation and if the gangrene, though wet, is not spreading rapidly, it is sometimes possible to inhibit it by the use of douches of very **hot, but dry, air** (at 300° C.—572° F.). These are not as painful as one would expect, and are repeated twice a day. It then becomes possible to amputate the limb under safer conditions.

Measures may be taken to promote circulation both in the involved and the as yet uninvolved tissues, such as **massage, local warmth, or diathermy**. Stetten has advocated **Bier's hyperemia**, the administration of **sodium or potassium iodide** for their absorbent properties, and **nitroglycerin** as an arterial dilator. Immersion in **hypertonic salt solution** is also advised.

Five cases of moist gangrene of the leg and 1 of the scrotum, all in diabetics, were completely cured by **diathermy**, irrespective of whether insulin was used or not. An 800 ma. current, with tin-foil electrodes, was used, each sitting lasting 30 minutes. Treatments were given 3 times weekly at first, then at longer intervals. Diathermy may preclude the need of amputation. Cluzet and Chevallier (Bull. de l'Acad. de médecine, Oct. 7 1924).

An important procedure is restoration of the urine and blood sugar concentration to normal by a suitable **diet**, together with **insulin** if indicated. Some advocate "feeding up" by an increase of the diet, including carbohydrate, to a level exceeding that for the uncomplicated diabetes,

as much insulin being given as is needed for proper utilization of this diet. Insulin does not lower the mortality from gangrene as much as that from diabetic coma, but nevertheless has exerted indirectly, according to Blotner and Fitz, a profound influence on the surgical problems involved by completely changing the dietetic management.

Out of 73 cases of diabetic gangrene, 13 were treated medically without insulin, with 3 deaths, and 40 surgically without insulin, with 10 deaths; 11 were treated medically with **insulin**, with 2 deaths, and 9 surgically with insulin, with 1 death. Thus, of 53 treated without insulin, 30 per cent. died, and of 20 receiving insulin, 15 per cent. died. Except for some cases of superficial gangrene, however, there were few which healed spontaneously under medical care alone. In brief, insulin permitted rapid desugarization before operation and a liberal diet in convalescence; patients were discharged sooner and in better condition. Blotner and Fitz (Boston Med. and Surg. Jour., June 24, 1926).

In operating for diabetic gangrene, especial care as to asepsis should be observed, and the intervention carried out simply and rapidly, with a minimum of trauma. A careful preliminary study of the circulation in the involved limb should be made. Healing is often slow, although somewhat accelerated by insulin.

There is a definite and important **prophylaxis** of diabetic gangrene. It consists of the avoidance of minor injuries (especially of the feet, as by tight shoes, stubbing the toes, or too thorough chiropody), of cold hands and feet, and of too sedentary a life. **Warm foot baths** may be taken and **exercises** of the toes and ankles carried out several times a day to enhance circulation through the feet.

**COMPLICATING INFECTIONS.**

—Carbuncles and furuncles not infrequently occur in diabetes. They should be treated by the methods in use for similar disorders in non-diabetic patients, with the added use of an appropriate **diet**, together with **insulin** when indicated.

According to King, boils in diabetics, when taken early, may often be aborted by rubbing in a 2 per cent. ointment of **yellow oxide of mercury** in lanolin. Where they persist, **tonics**, **vaccine**, **antiseptics**, **free drainage**, and sometimes **excision** are valuable. In carbuncles, in cases where the tissues show but slight resistance, early **excision** is best. Kolipinski, in carbuncle, favored precipitated **sulphur**, applied as a powder into the points of suppuration or ulceration, or used as an ointment with a cacao-butter base (1:8). In diabetic gangrenous ulcers Hartzfeld found useful **sodium perborate**, applied as a powder, usually twice daily.

Intercurrent infections such as rhinitis, pharyngitis, tonsillitis, bronchitis, pneumonia, appendicitis, inflammations of pyogenic origin, etc., reduce the carbohydrate tolerance of diabetics and are prone to bring on acidosis and sometimes coma, even in mild diabetes. These further complications can be avoided by the administration of **insulin**, or an increase in its dosage where it is already being given. The condition of the urine and blood should be carefully watched and the amount of insulin adjusted according to indications. The carbohydrate intake should be maintained even where the appetite is poor, by giving such foods as orange juice, milk, bread and cereals, which embody much carbohydrate in a relatively small bulk; enough insulin should be provided to insure proper utilization of this carbohydrate material.

In diabetes complicated by tuberculosis or syphilis, **insulin** is of great importance. In the former disease it is especially valuable in permitting a more nourishing diet than could otherwise be utilized. Since it may produce a focal reaction, however, the initial dosage should be small.

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**DIARRHEAL DISEASES OF INFANTS.—DEFINITION—**

In itself diarrhea can be regarded as a symptom only, but it has long been customary and is still convenient to group under this name, used generally, all those disorders in infancy which have as their chief symptom an increased motor and secretory activity of the intestinal tract. Such increased activity may, in a few instances, be the result of nervous impulses reflected through the central nervous system, but in the great majority of cases it is occasioned by the presence of irritating material of a more or less noxious character in the canal. In many instances it must be regarded as one symptom only of a systemic intoxication arising from the absorption of the toxic products of pathogenic micro-organisms developed in the alimentary tract; a symptom important in itself, but not to be considered apart from other symptoms of systemic disturbance, such as fever, quickened and enfeebled cardiac action, and nervous prostration.

In some instances, diarrhea must be regarded as a symptom of Finkelstein's "food intoxication," a disturbance of metabolism due to the ingestion of sugar and fat in larger



amounts than the infant's digestive tract can manage.

Inflammatory changes more or less extensive in character develop with varying promptness in the intestinal mucous membrane, in all the more severe diarrheas the result in some measure of the irritating character of the intestinal contents, but in a much greater degree due to a specific action of the bacterial toxins. Not infrequently the bacteria themselves penetrate the tissues of the intestinal wall, inducing destructive changes, aggravating the symptoms, and indefinitely retarding recovery.

All diarrheas involve some impairment of general nutrition; in severe or prolonged attacks the emaciation may become extreme.

Infants under the age of 30 months are peculiarly prone to diarrheal disorders; the mortality in New York City of infants under 2 years, from diarrheal diseases alone, exceeds the total number of all deaths from the infectious diseases of childhood (Holt). In them, to a much greater extent than in older children or in adults, has the disease a tendency to run a severe course, and to terminate fatally. For this reason the etiology and treatment of these disorders demand careful consideration.

**ETIOLOGY.**—If we inquire into the causes which induce this special liability to diarrheal disease on the part of infants a few facts stand out prominently.

**The Season.**—Diarrhea takes a comparatively unimportant rank among infantile disorders during the cooler months of the year. With the onset of warm weather, however, diarrhea suddenly acquires importance, owing to the frequency with which it is en-

countered, to its severity, and to its large mortality. This is evidenced by the statistics of all large cities in the temperate zones. Whenever the minimum temperature of the atmosphere for the twenty-four hours reaches the neighborhood of 60° F., diarrheal disorders assume the character of a widespread epidemic, an epidemic which reaches its height during the months of June, July, and August, and gradually subsides with the oncoming of cooler weather. Unquestionably the depressing effect of high temperatures upon the nervous and especially upon the vasomotor system of the infant plays an important part in the etiology of these disorders. Much more important, however, is the effect of continued heat on the development of bacteria in food materials which may be used for feeding the infant and especially in cows' milk; of this we speak later on.

It is probable that bacteria play a part in summer diarrhea, but the bacterial toxicity of milk is not proved, and there is not any just analogy between the disorders due to toxic products in the milk which affect all persons alike and the condition of summer diarrhea of infants. I. A. Abt (Jour. Amer. Med. Assoc., Oct. 28, 1911).

Czerny showed that accidental infections of nurslings can strongly affect nutrition. This kind of reaction may be initiated by vomiting with resulting loss of weight. Thus if an infant suffers from pyelitis of the relapsing type, or it suffers from follicular tonsillitis or grippe, gastric symptoms may be so prominent that the chief treatment may be dietetic. In these cases we may see constipation, although as a rule the infection causes increased peristalsis and excretion of mucus. The most common parenteral infections are grippe, pyelitis, furunculosis, phlegmons, umbili-

cal infections, cerebrospinal meningitis, and pneumonia. These are all coccus infections which have a marked tendency to implicate the intestines. Bernheim-Karrer (Correspond.-Bl. f. schweizer Aerzte, Mar. 17, 1917).

In children suffering from gastroenteritis or atrophy, 23 out of 26 gave a definite intradermal reaction to lactalbumin of the cow. Three reacted positively to caseinogen. The much greater reactivity to lactalbumin is in agreement with the observation that almost all allergic milk reactions proceed better with lactalbumin than with caseinogen. Greer (Arch. of Pediat., Nov., 1917).

The usual procedures of examination of gastric contents, stools, and the urine fail in many instances to supply the information necessary for a successful management of the patient. Several years ago the writer began X-ray studies of all cases that were difficult. In 57 patients the conditions found in the stomach series were dilatation, ptosis, pyloric spasm, pyloric obstruction (organic), and hypertonicity. In the study of the stomach and small intestine a mixture of bismuth, 1 part, to 8 parts of farina or cream of wheat gruel was fed to the child, and the radiogram taken at intervals subsequently. For the study of the large intestine a barium mixture was introduced into the lower bowel and after reverse peristalsis had carried the medium through the large intestine to the cecum, the radiogram was taken. The symptomatology of the stomach cases consisted in stomach pain (moderate or extreme colic), vomiting at intervals, rumination, cribbing, accumulation of gas (moderate or excessive), habitual loss of appetite, convulsions, chronic urticaria, secondary anemia, and failure to grow. The intestinal abnormalities included the following: Dilatation of the colon, localized sacculations of the colon, ptosis of the colon, adhesions of the colon, sacculations of the cecum, sacculations of the sigmoid, dilatation of the sigmoid, dilatation of the rectum, rectal

prolapse, and abdominal tuberculosis. The intestinal symptomatology included abdominal distension, chronic constipation, chronic diarrhea, intestinal colic, interval vomiting, persistent slight elevation of temperature, secondary anemia, developmental defects (physical), and mental irritability. With dilatation and sacculations of the sigmoid one was very apt to find derangements of peristalsis in the stomach which sometimes amounted to dystalsis; the peristalsis did not begin at the cardiac end of the stomach and proceed rhythmically, and there resulted a pylorospasm. C. G. Kerley (Med. Rec., Jan. 25, 1919).

The writer, summoned to Waterloo, 60 miles from Montreal, encountered therein an epidemic of hemorrhagic diarrhea due to the *Streptococcus mucosus*. The first case occurred on March 22d, 5 on the following day, and after that the number had increased to 65 in the town itself and there were other cases within a short radius. Adults composed about one-fourth the entire number. The larger proportion of cases, however, occurred in children under the age of 6 years. The attack began abruptly with high fever, nervous symptoms, and vomiting, and diarrhea set in early. Mucus and blood appeared in the stools and the amount increased rapidly as the stools became more frequent, and in the severe cases seemed to form almost all of the stool. Blood was a prominent feature in the stools in sixty per cent. of the cases. The attack lasted from a few days to 12, 14 or even 21 days. The temperature in the severe cases went as high as 106° (41.1° C), while in the milder cases it was comparatively low, 100° or 102° F. (37.8° or 38.9° C). In a few cases there was no rise above normal. Notwithstanding the severity of the cases no deaths occurred. Examination of the stools in one case showed large numbers of chains of *Streptococcus encapsulatus*, and about an equal number of colon bacilli. There were very few other bacteria.

There were no organisms of any of the types of *Bacillus dysenteriae*. In a second case examined there were large numbers of the *Streptococcus mucosus*. In searching for the origin of this epidemic an inspection had been made of the milk supply, but a careful study of the situation seemed to eliminate milk as the source of infection. The water supply came from springs and several of these were thought to be insufficiently protected against contamination. The epidemic occurred after a few days of pronounced warm weather when the snows were melting rapidly on a frozen soil.

The presence of such large numbers of the *Streptococcus mucosus*, associated with other streptococci and equal numbers of colon bacilli, and the absence of any *Bacillus dysenteriae*, indicated that the streptococcus must be regarded as the chief organism causing the epidemic. A. D. Blackader (Trans. Amer. Pediat. Soc.; N. Y. Med. Jour., Dec 18, 1920).

The writer ascribes to the Welch bacillus the phenomena of toxic gastroenteritis in infants. Its spores are introduced by the milk, and it develops a poison in the presence of sugars, probably *in vivo* as well as *in vitro*. Therefore he deems it rational to exclude carbohydrates from the food in such conditions. Jørgensen (Jahrb. f. Kinderheilk, Dec., 1925).

**Age.**—An investigation of the age of children thus attacked reveals the fact that the great majority are under 2 years. Holt recorded statistics of 3000 cases of diarrhea treated in family and dispensary practice, classified according to age. These showed that, of the total number, infants under 6 months formed 14 per cent.; infants from 6 to 12 months, 29 per cent.; infants from 12 to 18 months, 24 per cent.; infants from 18 to 24 months, 17 per cent., and children over 2 years, 16 per cent. In France, Lesage places

the age of special liability as under 18 months, and regards the first three months, and the period between the eighth and ninth months, when weaning is generally commenced, as specially dangerous.

**Overfeeding and Indigestible and Contaminated Food.**—It is the experience of every physician who has kept a record of his cases that fatal, or even severe, cases of diarrhea among infants fed entirely at the breast are extremely rare. Holt emphasized this when he said that of 1943 fatal cases of which he had collected records only 3 per cent. were breast-fed exclusively. He referred the partial immunity which, according to his statistics, infants under 6 months enjoy to the fact that the great majority of such are breast-fed, and in this way obtain a sterile and digestible food with little liability to overfeeding. With the commencement of artificial feeding, gastrointestinal disorders at once acquire prominence. Too often the food substituted for breast-milk is difficult of digestion, defective in composition, and given to the infant at too frequent intervals or in too large amounts, thus setting up indigestion and weakening the resistance of the intestinal tract to infection; nevertheless, as the experience of all testifies, the material supplied as food to the infant may be of a most faulty character, giving rise to indigestion, colic, and malnutrition, and yet during the cool season diarrhea, except of a temporary and easily controlled form, is rarely met with.

The carbohydrates, especially sugar, have more lately been incriminated as prominent causes during warm weather.

For the chief exciting cause, there-

fore, of the severer diarrheas of infancy we must look farther, and such a cause, it is now generally conceded, exists in the development in the intestinal tract of toxin-producing bacteria introduced for the most part with the infant's food. The most important ingredient of an infant's food is milk, and this is particularly liable to be contaminated from many sources. Even in winter the average dairy milk is loaded with micro-organisms, but their development is checked by the low temperature. With the approach of summer, however, and the raising of the temperature at which milk is kept to 60° F., multiplication of these organisms takes place with great rapidity.

The management of the diet is the most important factor in treatment. The first step is the immediate and complete **withdrawal of food** at the beginning of the attack. The second step is the removal of any food already in the intestines. **Castor oil** or **magnesia** are advised to accomplish this. If there is vomiting, it may be necessary to wait for its subsidence before giving the purgative. A large **intestinal douche** can, however, be given at once. The length of the period of starvation depends upon the case. A breast-fed baby may be kept from suckling for 24 hours. Bottle-fed babies usually require a longer time. **Water** should be given freely, and it is often a great relief to the mind of the mother if she is allowed to use **barley water**. So long as the fever remains, showing that an infection is still present, resumption of the milk diet should be delayed. When it is started, it should be given in small quantities, diluted and preferably skimmed, and the return to the original strength should be made gradually. An excess of fat or sugar may cause diarrhea. **Broths** thickened with starchy substances or even thick **porridges** are of great value when

the time for the return to food has come and the action of the milk is feared. In obstinate cases it is sometimes best to abandon the milk mixture and to use **whey**, **casein milk**, **buttermilk**, or the like. The thick gruels are very valuable as foods. On account of the starch, it is not advisable to continue their use over long periods. On account of the danger of relapse and recurrence restriction of the diet should be continued for the duration of hot weather. Gain of weight in these cases becomes of minor importance for the time. Acidosis is one of the great dangers during diarrhea. J. P. Crozer Griffith. (*Arch. of Pediat.*, Aug., 1920).

In the adult the acidity of the gastric juice and the more complete digestion of the food in the stomach check the development of micro-organisms before the food enters the intestinal tract. Traube and Eschrich have shown that in the infant stomach this inhibitory action is, to a great extent, wanting. During the digestive act there is no free hydrochloric acid in the infant's stomach. Both digestion and absorption take place more imperfectly in the stomach of an infant than in that of an adult and the food is quickly passed on into the small intestine, where it meets the bile and the alkaline secretions of the duodenum. There is now practically no hindrance to the development of injurious bacteria, excepting in the rapidity and completeness with which the digestive process is performed. Imperfect digestion, always slow digestion, therefore, by permitting fermentative changes furnishes the conditions under which pathogenic bacteria, introduced by means of contaminated food, or present in the canal, but previously hindered in development, may flourish and evolve their poisonous toxins.

Booker, to whom the medical world is indebted for a careful investigation of this subject, states that in infantile diarrhea the conditions for the development of bacteria in the intestinal canal appear to differ from those obtaining in the healthy intestine. The bacterial forms present a greater variety; forms met with only occasionally and in small numbers in the healthy intestine are now much more pronounced, and frequently appear in immense numbers, while the *Bacillus coli communis* and the *Bacillus lactis aerogenes* become more uniformly distributed through the intestine. No single species of micro-organism is met with sufficiently frequent to be regarded in itself as the specific cause of diarrhea; but among the many forms encountered several varieties of streptococci and the *Proteus vulgaris* appear to be of special importance. The streptococci are met with frequently; rarely seen in the stomach and upper part of the small intestine, they become much more abundant in the lower ileum and colon, especially in those cases where ulceration of the mucosa is going on. So constantly and in such large numbers are they found in these cases that it is reasonable to suppose that they play an active and important rôle in the ulcerative process. Of the *Proteus vulgaris*, Booker says that it is found in more than half of the severer cases of diarrhea; in the milder forms it is seldom seen. Cases in which this bacillus abounds present a different type of symptoms to those in which streptococci prevail; the patients more frequently show toxic phenomena and have watery or semifluid stools with a strong, of-

fensive odor, but otherwise exhibit little evidence of serious inflammatory trouble in the intestine. More recently considerable attention has been devoted to an investigation of the *Bacillus dysenteriae* and the part it plays in the production of dysentery. It was first studied by Shiga, and afterwards by Flexner in the Philippine Islands, both of whom found it present in such a large proportion of the diarrheas of the East as to suggest a causal relation. Two distinct and important varieties have been noted, which have been named after these two investigators. More recently it has been recognized as present in a larger number of the dysenteric diarrheas in this country. A careful investigation at the Rockefeller Institute in 1903 of 412 cases of summer diarrhea showed the presence of this micro-organism in 270 cases. It was almost invariably found to be present in those cases characterized by the presence of mucus and blood in small quantities. Associated with this bacillus are numerous streptococci and bacilli of the colon group. Among other forms of bacteria possessing pathogenic properties encountered we may mention the *Staphylococcus pyogenes*, the *Bacillus pyocyaneus*, the *Bacillus mesentericus*, and the *Bacillus enteritidis* (Gärtner). Such forms probably more or less modify the symptoms.

Clinical value of **fruit juices**, especially **orange, grape, apple** and **peach juices**, emphasized. Zahorsky (Mo. State Med. Assoc. Jour., Aug., 1920).

The disturbance of nitrogenous metabolism caused by intestinal microbes in nurslings is relatively slight. The only striking change caused by the mixed flora was a marked fermentation of utilizable carbohydrates, with rapid

formation of acid—principally lactic. Kendall, Day and Walker (Jour. of Infect. Dis., Mar., 1926).

**Depressed Vitality.**—We may add that all conditions which lower the vitality of the infant favor gastro-intestinal disturbance and impair the infant's resistance to infection. The intense heat of summer, especially when associated with great humidity, exerts a depressing action upon the nervous system of the infant, particularly upon the vasomotor system, and must, we think, be regarded as an important predisposing cause. Defective hygienic conditions, previous acute disease, and malnutrition in all its forms, especially if associated with rachitis, syphilis, and tuberculosis, act in this way. All forms of overexcitement, the nerve irritation often accompanying denitition, and reflex impulses arising from undue exposure of the lower limbs and often the abdomen of the infant to variations in temperature have all a disturbing influence in digestion, and may, therefore, be regarded as predisposing causes of diarrhea. Still more, if these conditions continue, or are frequently induced, this repetition of "insults to the intestinal mucosa" (Flexner) renders the intestine particularly liable to bacterial invasion.

**MORBID ANATOMY.**—The anatomical lesions met with in the intestinal tract of the infant, as the result of diarrhea, are of a varied character, and are due, apparently, to the intensity of the irritant and the period of time during which its action has persisted. Nevertheless, it must be acknowledged that there is frequently a surprising want of relation between the post-mortem evidence of disease and the severity of the clinical phenomena, and *vice versa*. At-

tempts have been made at a classification, but it is generally admitted that, although cases may be grouped according to the prominence attained by certain lesions, no distinct dividing lines can be drawn.

In the acute cases the lesions may be comparatively superficial. In such to the naked eye the stomach and upper portion of the small intestine appear almost normal; toward the lower end of the ileum and throughout the colon, indications of inflammatory disturbance may be seen; as a rule such are specially pronounced in the region of the sigmoid flexure. If the attack has been severe, irregular patches of local congestion are seen, with more or less swelling and hyperemia of the solitary glands and of Peyer's patches. Under the microscope hardened sections of the intestinal wall show in places loss of superficial epithelium, due, in great measure, to the irritative action of the toxins generated by the bacteria. Wherever this erosion has taken place an invasion of the mucosa may follow. This condition is especially noticeable toward the lower portion of the ileum and over the whole of the colon, where a considerable infiltration of the mucosa may frequently be seen. In a few instances signs of an acute general infection are presented by fatty degeneration and necrosis of cells in the liver, by the presence of lobular pneumonia, and by necrosis of the epithelium in the convoluted and irregular tubules of the kidney.

The result of experiments by the writer shows that the glycolytic power of the tissues of the nursling is relatively high, since the quantity of sugar so convertible varied between 50 and 80 cm. per kilogram of weight, while the liver arrests only about 4 or 5 Gm.; that inversely with

what is observed in the liver the glycolytic power of the tissues remains about constant, whether the experiment be made upon a healthy infant or upon one suffering from gastroenteritis; that, consequently, it is not necessary to take into account this possible source of error in investigating alimentary glycosuria in the nursling. Terrien (*Revue mensuelle des mal. de l'enfance*, Jan., 1901).

The urinary findings in a series of infants under constant observation in hospital wards showed that in 22 the urine was abnormal; it contained albumin and occasionally hyaline casts as the only pathological element in 7 instances (febrile or toxic albuminuria); in 7 others the presence of pus cells was the chief characteristic (pyuria-pyelitis); in the remaining 8 cases albumin, casts, and pus were all present, indicative of nephritis or pyelonephritis. The urinary changes were more frequent in ileocolitis than in dyspeptic or fermental diarrhea, though the extent of renal involvement seemed to depend less on the variety of the intestinal infection and more on its intensity. The pyuria persisted in some instances without apparently interfering with convalescence; in others it yielded to urotropin, and in still others it developed into a serious and fatal complication. The infection seemed to have its origin in the intestinal canal, whence it reached the kidney either through the blood- or lymph- streams or by contiguity of structure. There was no evidence of involvement of the urethra or bladder or of ascending infection. The few autopsies made indicated clearly that although the kidneys frequently escape injury during enteritis, they become the seat of extensive secondary changes in this as in other forms of infection. The renal changes during intestinal diseases in infections seemed to be those of degeneration (parenchymatous, hyaline, and fatty) of the convoluted tubules rather than those of focal infection. In 19 cases suffering

from ailments other than intestinal infection, and for the most part less acute in character, no urinary abnormalities were discernible. J. H. M. Knox and J. C. Meakins (*Arch. Int. Med.*, vol. ii, p. 241, 1908).

Hohlfeld, in a number of investigations, found that in the majority of fatal gastroenteric cases the urine contained albumin and a few casts. In 35 autopsies the changes in the kidneys were found to be parenchymatous. He believes that toxemia and kidney irritation react on each other and offer a bad prognosis. Chapin, in 86 cases, records 75 as having albumin and casts in the urine; also the majority of the fatal cases had albumin in the urine. The authors tested the urine in 300 babies suffering from gastrointestinal conditions. The writers conclude that the pathological condition in the kidneys does not progress beyond cloudy swelling or acute hyperemia. There was nothing to suggest any relation between the kidneys and stupor, restlessness and convulsions. These they believe are due to toxemia and not to uremia. J. L. Morse and Bronson Crothers (*Arch. of Pediatrics*, Aug., 1909).

In cases of acute intoxication the writer found that the intestinal mucosa contained a poison which, on injection in animals, produced depression and narcosis, anorexia, circulatory failure, diarrhea, and sometimes convulsions and death. Young animals were especially susceptible to it. Crystals resembling those of the dipicrate of beta-aminazolyethylamine were obtained from the mucous membrane; on prolonged boiling with alcohol to restore their basic character these became highly toxic to animals. Previous dehydration of an animal made it more susceptible to the poison. Portal blood from patients was also very toxic to animals; systemic blood, less so. Boiled extracts of fresh stools proved non-toxic. G. L. Boyd (*Arch. of Int. Med.*, Feb., 1923).

In another class of cases the inflammatory changes are more pronounced.

In a proportion of these the lesions may be described as catarrhal in character. The macroscopic changes are, to a great extent, confined to the lower end of the ileum and to the colon, where the congestion may be very marked; in some cases quite general; in others localized in patches. The lymph-nodes are enlarged and can frequently be seen with commencing ulceration at their summit; Peyer's patches are swollen and hyperemic. Under the microscope hardened sections from the stomach and the small intestine reveal marked cloudiness of the epithelial cells, and in places loss of superficial epithelium. The connective tissue of the villi and that supporting the glands of Lieberkühn are more or less densely infiltrated. The ducts contain an excess of goblet-cells and are distended with mucus. The loss of superficial epithelium is extensive throughout the colon. Associated with it is a more or less dense infiltration of the mucosa, an infiltration which, in places, may extend even to the muscular coat. Should the duration of the attack be further protracted, ulceration may supervene, chiefly in the colon, rarely in the lower portion of the ileum. Such ulceration is, for the most part, superficial, rarely extending deeper than the mucosa. The ulcers, in general, are circular, but in the more severe cases several ulcers may coalesce, forming large, irregular patches, two to three inches in diameter.

In the cadavers of 10 infants the inflammation in the intestinal mucosa had been mainly restricted to the ileocecal valve. It rarely extended into the small intestine and then but a short distance. In the large intestine the inflammation spread more. In a few cases there was slight inflammation in the duodenum, but, as a rule, the small intestine was free

from any decided inflammation. The superficial epithelium and the glands were generally in good order. C. E. Bloch (*Jahrbuch f. Kinderheilkunde*, Bd. lviii, No. 5, 1905).

In another group of this class the intensity of the inflammation appears to fall chiefly upon the lymph-nodes, which throughout the colon, and especially in the neighborhood of the sigmoid flexure, show indications of a destructive inflammation. Under the microscope they are seen to be swollen and infiltrated, many showing focal necroses. The surrounding tissues are deeply infiltrated with lymphoid cells. In time they break down, forming small, but deep ulcers, with overhanging edges, exhibiting a tendency to extend chiefly in the submucous tissue. In a few cases, fortunately rare, the inflammation of the colon is of such an intense fibrinous character as to lead to necrosis with the formation of pseudomembrane.

A blood change which stands out prominently is the relative increase in the polymorphonuclears and the decrease in the lymphocytes. This is of importance, because it is found to be of value in prognosticating the severity of the attack. A marked increase in the number of polynuclear leucocytes means that the child is badly poisoned, whatever the other signs may indicate. J. Zahorsky (*N. Y. Med. Jour.*, Sept. 12, 1903).

Determinations of the H ion concentration and of the tryptic and amylase activity in 49 specimens of the gastric contents from normal infants and others convalescing from diarrhea showed that diets of some form of lactic acid milk increased the gastric acidity. There was, however, very little evidence that either these diets or the resulting increased gastric acidity destroyed many organisms in the stomach. The acidity of specimens collected less than 6 hours after a meal was higher than that of the specimens obtained later. Elevation of the body



temperature and the presence of vomiting increased the gastric acidity. Practically no difference could be found in the reaction or cultures of the gastric contents of normal infants and of those convalescent from diarrhea. Davison (Am. Jour. Dis. of Childr., July, 1925).

**CLASSIFICATION.**—Attempts have been made at a classification of diarrheal disorders, based either upon the changes found *post mortem* in the intestinal canal or upon the bacteriological conditions met with in the discharges, but in both respects our knowledge is still too imperfect to permit us from it to draw dividing lines in a satisfactory manner. Attempts have also been made to recognize certain clinical types of the disease, but it must be admitted that our clinical types have no sharp dividing lines, and, both in the group and in the individual, they show a tendency to pass from the milder into the more severe form.

Two classifications, which rest partly on a pathological and partly upon a clinical basis, are worthy of mention. One is that of Lesage, who groups the acute cases of infantile diarrhea into three classes. In the first he includes all those which are due to the presence in the infant's food, whether breast- or cows' milk, of irritant substances not the result of fermentation in the milk. These diarrheas are generally of a mild type and quickly controlled. In a second group are placed those cases where the disturbance is due to fermentation in the stomach or intestinal canal of indigestible, but at the same time more or less sterile, food. The constitutional intoxication in these cases is due to the abnormal development and some times increase in virulence of bacteria previously existing in the canal (endogenous). These cases, although

sometimes severe, generally run a comparatively mild course. The third and largest group contains all those cases in which the diarrhea is due to bacteria and their toxins present in the milk administered as food to the infant (exogenous). The constitutional symptoms met with in this class are frequently of the severest type.

Booker also groups the acute cases of diarrhea met with during summer into three classes. In the first he places all cases of a dyspeptic and non-inflammatory character. In these the stools are lumpy, acid, and contain no leucocytes or epithelial cells; the bacteria are only those of normal healthy motions, and the diarrhea is of a mild form and, for the most part, easily controlled; however, if neglected, it shows a tendency to take on the characters of one of the two succeeding classes. The second group is characterized chiefly by symptoms of a systemic intoxication, with which is associated a variable amount of local inflammation; the stools are frequent, much altered in color and consistence, and contain curds and an increase of mucus. Seldom any one form of bacteria is so greatly in excess as to exclude the influence of other forms. In a third group of cases local inflammatory symptoms are prominent; the stools are frequent, contain much mucus, and sometimes blood; streptococci are found in predominating numbers, although other forms of bacteria are also present. In the more severe cases an invasion of the tissues of the intestinal wall by bacteria takes place, and in many instances more or less extensive ulceration of a suppurative character may be found *post mortem*. There is, according to Booker, a considerable difference in the clinical course run by the individual cases in

this group; some patients respond readily to treatment, while others are little influenced and steadily grow worse, until the disease terminates fatally. Booker thinks that this may possibly be due to the fact that the streptococci met with are of more than one variety.

While typical instances of these three groups may be easily recognized, there are many transitional cases which do not fall into any one of them, and are probably due to a more mixed infection in which no one micro-organism is especially predominant.

This classification of Booker's corresponds clinically very closely with that of Holt, who, however, lays more emphasis on the anatomical post-mortem changes.

To these groups we must add a fourth, comprising those cases which assume a chronic type, and are not infrequently met with as the sequelæ of one of the preceding forms. With this group, as with the others, we can draw no definite dividing line separating it sharply from the more acute cases. Holt terms those cases chronic which have persisted longer than six weeks. Some cases, however, beginning acutely, assume the type of chronicity sooner even than this. In these the activity of the inflammation subsides, the appetite partially returns, but the diarrhea though lessened persists; in some maintained by a varying amount of ulceration of the intestinal wall; in others by a more or less atrophic condition of the intestinal glands. In the latter case the progressive emaciation indicates how serious is the interference with the processes of digestion and absorption.

These somewhat provisional groups may be tabulated as follows:—

1. Functional diarrheas non-inflammatory in character.

2. Inflammatory diarrheas in which the symptoms of a toxic systemic infection are predominant.

3. Inflammatory diarrheas in which, in addition to the systemic infection, the symptoms of an acute local inflammation have a prominent part.

4. Chronic diarrheas in which the acute inflammatory symptoms have more or less subsided, but in which the stools remain abnormal, both in character and frequency, and emaciation is apt to supervene.

#### FUNCTIONAL DIARRHEAS.—

Many cases of infantile diarrhea are met with which must be regarded as functional rather than inflammatory in character. During dentition a moderate increase in peristalsis and secretion is sometimes noted which it is difficult to attribute to any fault in diet, and which promptly subsides on the eruption of the teeth. In a few instances a similar condition may be induced by impulses acting through the nervous system, such as fright, overexcitement, and a sudden chill to the surface of the body. At other times these same causes act chiefly by disturbing digestion. Substances also may occasionally be given as food to the infant which act as direct mechanical irritants to the sensitive mucous membrane of the alimentary tract.

In this group are also to be placed many diarrheas met with in breast-fed infants, where, owing to a faulty dietary or mode of life, or to a nervous overstrain on the part of the mother or nurse, the breast-milk becomes altered, resulting in either gastric or intestinal indigestion in the infant, followed by diarrhea. The time of weaning is apt to be associated with a similar irritability. This liability is still further increased by all conditions which lower the tone of the nervous centers.

**Symptoms.**—In some instances the diarrhea may commence quite suddenly with large, more or less fluid motions, containing, besides fecal matter, considerable undigested material. In other cases symptoms of gastric irritation and abdominal pain precede, for some hours, the diarrhea. Examination of the infant generally reveals a moderate amount of pyrexia:  $100^{\circ}$  to  $103^{\circ}$  F. ( $37.8^{\circ}$  to  $39.4^{\circ}$  C.); rarely does the temperature run higher, except in cases of sudden onset with severe gastric disturbance. Slight abdominal distention may often be noted. The stools are frequent, thin, usually sour-smelling, and of varying color. In young infants on an exclusive milk diet they are, in general, of some shade of green and of a distinctly acid reaction; occasionally, however, they are gray or chalky in color and frothy in character. In older infants on a more mixed diet the stools may have no uniform color, but be in part green and in part some shade of brown. Undigested food is always present in the form of casein masses, or smaller and softer masses, consisting of fat curds or soap. Examination of the stools under the microscope reveals only those forms of bacteria met with in normal feces. The infant is peevish and may either refuse its food altogether or drink greedily only to allay its feverish thirst. Should the pyrexia run high, nervous symptoms may manifest themselves, *e.g.*, twitching of the limbs, great restlessness, and wakefulness.

Food fever in children consists of an attack of fever which comes on suddenly, is accompanied by signs, more or less pronounced, of digestive disturbance, lasts in its acute form for several days, and may linger on in a modified degree for some weeks. If the attacks occur frequently, once

a month or so, their effect upon the nutrition of the patient is highly injurious. The subjects of the complaint are usually neurotic children of either sex between the ages of 3 or 4 and 10 or 12 years. The attack begins with headache, sometimes with vomiting, sometimes with diarrhea. The temperature rises to from  $101^{\circ}$  F. to  $105^{\circ}$  F. ( $38.3^{\circ}$  C. to  $40.5^{\circ}$  C.); it is usually reduced by a dose of **calomel**, but rises again. Smith (Brit. Med. Jour., Feb. 10, 1906).

"Soapy stools" indicate always some chronic disturbance in the absorption of fat. At the same time the splitting of the fat proceeds unhindered, and there cannot be much acidity or increased peristalsis or catarrhal irritation. Hecht (Münch. med. Woch., May 12, 1908).

Large curds in infants' stools are composed of some protein (probably casein or one of its derivatives) which, on coagulating, entangles the milk fat in its meshes. The amount of fat in the curds depends on the amount of fat in the milk, and as this fat increases it replaces the protein in the curd. The presence of large curds, which has been taken by some investigators to indicate an increase of gastric HCl, can with as great probability be interpreted as indicating a lack of HCl. Talbot (Boston Med. and Surg. Jour., June 11, 1908).

Diarrhea in the breast fed the first days of life may be due, according to Marfan, to hypersensitization of the intestine to the maternal milk. The affection is not grave, never inducing marasmus. **Toasted bread tea**, *i.e.*, toasted slices of wheat bread ground and sifted, 2 teaspoonfuls boiled in 100 Gm. ( $3\frac{1}{2}$  ounces) of weak tea sweetened with a little sugar or saccharin, is given before each feeding 4 or 5 times a day. Improvement occurs in 2 or 3 days. By the second to the fourth day there are no more than 3 or 4 stools daily. The infant regains appetite and gains in weight. This method of feeding was sometimes continued by the writer until the infant was 3 months old. The breast feeding was never in-

errupted. Bytsch (Nourrisson, Jan., 1926).

The attack in this type of the disease is generally of brief duration. After the diarrhea has continued for twelve or twenty-four hours the temperature generally falls; nervous symptoms, if present, pass away; the motions in a few days become less frequent and gradually resume their normal appearance, and the desire for food becomes more imperative.

**Diagnosis.**—At the onset, unless from the history of the case, it is impossible to predict with certainty just what we may have to deal with. It must be remembered that symptoms similar to the above may not infrequently usher in a severe constitutional disorder.

**Prognosis.**—Simple functional diarrhea, unless in infants of the weakest constitution, can never be regarded as presenting much cause for anxiety. The danger lies in neglect. An injudicious dietary, especially in hot weather, may prolong the attack or convert it into one of the inflammatory forms of the disease.

**Treatment.**—In cases in which the diarrhea appears to have removed the irritant, it will suffice to secure absolute rest to the alimentary tract for a period varying from twelve to twenty-four hours, permitting only sterile water in small quantities as frequently as may be desired. In the majority of instances, however, it is wiser to secure at the outset, by means of medicine, a thorough evacuation of the bowels, ridding them in this way of any fermenting material. To accomplish this we may make use of either **castor oil** or **calomel**, both of which act promptly and with little irritant effect on the mucous membrane. Of the former a full

dose may be given in any convenient way.

Should there be much gastric irritation, as shown by a tendency to retch or vomit, the latter is preferable, and may be given in small doses ( $\frac{1}{4}$  to  $\frac{1}{4}$  grain—0.008 to 0.016 Gm.) at intervals of half an hour or of an hour until a decided effect is obtained. Afterward, if necessary, one of the preparations of bismuth, preferably **bismuth carbonate**, with a small quantity of some opiate, may be given for a few days. If the attack has been of a mild character, a thin **rice** or **barley water** containing a small amount of **sugar of milk** may be allowed after the first twelve hours have passed. Stimulants in the form of **whisky** or **brandy** are to be given only if indications of prostration make their appearance. In the majority of cases this dietary may be increased after thirty-six or forty-eight hours. In infants who are breast-fed, a limited nursing may be allowed, permitting the infant to take a little more than half its usual quantity at each nursing. **Rice water** or weak **albumin water** may be given between times. In those artificially fed the food for several days must be weak in character and limited in amount. A small quantity of a fat-free milk may be added to the rice or barley water after the third day.

The writer divides the micro-organisms which are the primary cause of diarrhea in bottle-fed infants into 3 main classes: the dysentery bacillus in all its forms, the gas bacillus and similar organisms, and thirdly, other bacteria, chiefly streptococci, the colon bacillus, and the pyocyaneus. The symptoms afford no clue as to the form of organism present, and nothing about the stools aids except, rarely, the peculiar green

color caused by the bacillus pyocyaneus and the streptococcus. In the former instance the green color will disappear on the addition of nitric acid, and in the latter streptococcus can usually be easily recognized by the microscope. The only affection with which a typical case may be confounded is intussusception.

Treatment should begin with a dose of **castor oil**, stopping all food from 12 to 24 hours, giving water freely.

In diarrhea due to the *dysentery* and *colon bacillus* and *streptococcus*, **carbohydrate food** is indicated. **Sugar** and **lactose** are better than starch, dextrin and maltose preparations. The **milk** should be given in **barley water**. Some protein food, exemplified in **whey** or **casein**, should be added gradually as soon as there is improvement. No fat should be given until actual convalescence.

In diarrhea due to *gas bacillus*, carbohydrates should be cut down and **acid-producing bacteria** introduced into the bowels; **buttermilk** or, better, mixtures containing 3 or 4 per cent. of **lactose** and from 1.5 to 2.5 per cent. of **protein ripened with lactic acid organisms**. At any given time most cases of infectious diarrhea are due to the same organism.

An unscientific, but often the only practicable method, is to give what seems to be the **most rational diet** and then observe the results. **Irrigation of the bowels** once or twice a day is useful, and if blood and pus persists in the stools after evidences of toxemia have disappeared, injections of **silver nitrate** may be of service. The various so-called intestinal antiseptics are of little or no value, and there is no serum. **Hot stupes** or **compresses** allay pain and tenesmus, though sometimes **opium** (preferably small repeated doses of **paregoric** or **Dover's powder**) is required. Stimulants such as **strychnine**, **caffeine**, and **camphor** are often called for. Morse (Amer. Jour. Med. Sci., Jan., 1915).

The three principal causes of diarrhea in infancy are too high a sugar

percentage in the food, too much food at a time, and bad milk. The important principle is to give a **food low in carbohydrate**. The writer recommends for babies under 6 months old a mixture of **skim milk and water** with enough **calcium casein** to bring the protein proportion up to 2.60 per cent.—giving the formula: Fat, 0.25; sugar, 2.25; protein, 2.60. For babies over 6 months old the same dilution of casein is added to 3 per cent. One-third of an ounce of powdered casein in a mixture of 16 ounces of skim milk and water is used, but the powdered milk and 16 ounces of water raises the protein proportion to 2.60 per cent. In a 48-ounce mixture, half skim milk and half water,  $\frac{2}{3}$  of an ounce of powdered casein raises the protein to 3 per cent. In general slightly smaller amounts are given than to a well baby. After a day or two the stools diminish in number, become more yellow, and after three to five days they become pasty, light yellowish brown in color, and alkaline in reaction. After the diarrhea has stopped, whole milk is added to make the fat proportion from 1 to 2 per cent., and if this is borne well, in two or three days enough sugar is added to make the sugar proportion about 3.5 per cent. **Malt sugar** is the best to use. L. W. Hill (Boston Med. and Surg. Jour., Apr. 6, 1916).

Certain cases showing recurrent symptoms of gastrointestinal disturbance, vomiting, fever, etc., do not respond to treatment usually effective in such cases. The X-ray has furnished the explanation. In some an elongated sigmoid was found, and in others a ptosis of the stomach; others again showed a partial pyloric stenosis. The bowels are cleared with **Russian oil**, **olive oil**, or **fluidextract of cascara**. A teaspoonful of the latter in 3 doses gives better results than when given at once.

**Massage and physical therapy** were found to be of the greatest aid in constipation due to the long sigmoid. The writer omitted white bread, crackers, and similar articles, and gave more green

vegetables and fruits, except in cases in which there was diarrhea. In cases with diarrhea he omitted the fruit and vegetables and gave boiled skimmed milk. C. G. Kerley (Med. Rec., June 24, 1916).

In a study of 220 cases observed in St. Louis during 1925 the writer emphasizes the dangers of *anhydremia*. He argues that there is a true toxic substance in the genesis of enteritis which evokes symptoms even when the water loss is small and the intake ample. The tissues refuse to retain water. The labors of Finkelstein and his school have overthrown the bacterial toxins as cause, while the rôle of sugar, salt and other substances, acids and alkalis, is deemed doubtful. Plantenga recently held that toxic intermediary products were the primary cause of the diarrhea, as instanced by the coli-toxin of calves which produces all the symptoms of intoxication observed in infants. J. Zahorsky (Mo. State Med. Jour., Mar., 1926).

General measures, such as physical rest, with freedom from all forms of excitement, **frequent bathing** with water graduated in temperature to suit the condition of the infant, and abundance of **fresh air** are all important in the management of these cases of functional diarrhea.

### **INFLAMMATORY DIARRHEAS: SUMMER COMPLAINT OF INFANTS.**

The two groups of inflammatory diarrheas include the great majority of cases of infantile diarrhea met with during the summer months. They are very closely allied in their etiology, and, although the intestinal lesions in the one are comparatively slight, while the symptoms of local inflammation in the other become prominent, in both we have to deal with marked constitutional disturbance. All that has been said in reference to the influence of age, of season, and of the mode of feeding is equally

true of both groups. The symptoms and course of these two varieties of the disease differ in important particulars.

### **INFLAMMATORY DIARRHEAS in which the Symptoms of a Toxic Systemic Infection are Predominant; ACUTE GASTROENTERIC INFECTION: ACUTE GASTROINTESTINAL CATARRH.**

**Symptoms.**—As might be expected, when we consider the various ways and the varying numbers and characters with which these toxin-producing bacteria make their entrance into the alimentary tract and the different conditions under which their development may take place in the stomach and intestine, the mode of onset of this disease is very variable. Frequently it is gradual; the symptoms present little except their persistence to distinguish them from those produced by indigestion. The infant may be fretful, show occasional signs of colic, be restless at night, and slightly feverish, and associated with these disturbances may be some looseness of the bowels. As the disease progresses the symptoms increase in severity; the motions become frequent, thin in character, of a sour, or, more generally, of an offensive odor; their color is variable, generally some shade of green, due to an alteration in the bile-pigment, the exact nature of which is still uncertain; pyrexia increases, the pulse becomes quick and weak, and pain becomes a marked feature, interfering with rest and sleep.

Green stools are distinguished not only by their color, but by the presence of considerable mucus. This is due to the action of a substance which the writer has isolated from such stools, and regards as a ferment. It oxidizes guaiacol in presence of hydrogen dioxide, but the reaction

does not occur if the stool is first heated to boiling point. The oxidation causes a brownish discoloration which is most marked in the flakes of mucus and is not diffuse. The substance is contained in the mucus and apparently has an oxidizing action on bilirubin. Wernstedt (*Hygiea*, vol. lxxvii, No. 8, 1905).

The degree of oxidation of the biliary coloring matter in the stools of infants does not depend wholly on the oxydase, but a distinct influence is exerted on the coloring by the very uncertain, but usually significant reducing power of the bacteria in the stool. The oxydase can certainly develop its action only when the reduction process is so insignificant that the biliary coloring matter is unaffected. If the reducing power is increased in intensity the stool always contains somewhat reduced biliary coloring matter, pre-eminently bilirubin. The intestinal bacteria then hinder the oxidation of the biliary coloring matter so that such stools contain bilirubin in spite of the amount of oxydases. Hecht (*Münch. med. Woch.*, June 11, 1907).

In other cases grave symptoms appear suddenly in an infant who has previously been well or only slightly ailing. The temperature rises rapidly to 104° or 105° F. (40° to 40.5° C.), with either unusual drowsiness or great restlessness, and signs of distress. Vomiting may set in early and continue in a most persistent manner. In some instances alarming nervous symptoms may develop, such as stupor, great excitement, or even convulsions. After several loose movements have occurred the temperature may fall 1 or 2 degrees, and the nervous symptoms pass off to a great extent. Frequent loose movements, with much colicky pain and considerable prostration, now make their appearance.

When the disease is well established

the symptoms become very characteristic: the infant is restless, moaning or crying frequently; the face is pale and its features somewhat pinched; the eyes sunken; the tongue coated in the center, but with tip and edges red and dry; thirst is pronounced, but fluids are frequently vomited shortly after they are taken; the abdomen is generally, but not always, distended. Occasionally we may distinguish through the thin abdominal wall marked distention of the stomach or of the small or large bowel. The skin gradually assumes a harsh feeling, while the subcutaneous tissues waste rapidly; the temperature varies from 102° F. (38.9° C.) in the morning to 103° F. (39.4° C.) or more in the evening, and the quick and feeble pulse indicates great exhaustion. Pain, to a greater or less extent, is always present, but exacerbations may be noted shortly before each evacuation. Abdominal tenderness is not marked, but exists in some cases. The stools continue to be frequent, often almost entirely fluid, and of a varying color, green or brown; they have a sour, more generally an offensive odor, and contain an excess of mucus. Little useful diagnostic information can be gained from their appearance, but we may consider that frequent and very fluid stools indicate a severe attack. The reaction is, in the beginning, always acid, but in the more severe cases becomes neutral or even alkaline. Lesage says that a relation generally exists between the character of the reaction and the degree of the infection. Under the microscope the stools are seen to contain undigested food, epithelial cells, few, if any, leucocytes, and numerous bacteria, among which bacilli predominate. As the disease progresses the vomiting becomes less urgent, the pain appears to be less

acutely felt, the pulse becomes weaker, emaciation proceeds rapidly, and the urine becomes scanty and not infrequently shows the presence of a small amount of albumin.

Should the disease proceed to an unfavorable termination the general prostration increases; the extremities become cold, slightly cyanosed, and sometimes edematous; the slightly swollen eyelids only half close over the deep-sunken eyes; the fontanelle, if still open, is much depressed; the infant ceases to cry, and death closes the scene generally in a very quiet manner.

Under wise and energetic treatment, however, begun early, the course of the attack may be aborted or much shortened, particularly in infants with a previously good digestive record. In some, although the severity of the symptoms may abate, the diarrhea persists and indications of a modified ileocolitis make their appearance.

Relapses are not uncommon, due, most frequently, to some error in dietary, usually that of allowing milk too early and in too strong a modification. Occasionally they appear to arise from the nervous and cardiac depression produced by a wave of intense heat.

**Complications.**—In the more severe cases complications are frequently met with. Unless care is exercised, thrush is apt to appear in the mouth and spread rapidly. While in itself of slight import, it may, owing to an accompanying stomatitis, still further increase the difficulties of feeding.

Symptoms in the respiratory system in many cases develop early. Fenwick states that in 87 per cent. of his cases signs of bronchitis were present at the end of the fourth day; pneumonic consolidation was encountered in 37 per cent. To us in America these figures

appear high. The onset of the bronchopneumonia is, however, often very insidious; the cough may be only slight, but the respirations will be observed to be unduly frequent, and the temperature shows a distinct rise. The physical signs are generally obscure, and most frequently are localized at the base of the lungs. The progress of the pulmonary lesion is modified by the general symptoms of the case; increased dyspnea is often a symptom of grave import. Pleurisy is very seldom observed; when it does manifest itself it tends rapidly to become purulent.

Associated sometimes with the pulmonary infection, but occasionally as a complication by itself, we meet with cerebral symptoms, stupor, delirium, or convulsions. Only rarely do we observe definite signs of local irritation, such as strabismus, inequality of pupils, and irregular pulse and respiration. Lesage makes reference to a form of paralysis which disappears with returning health. Thrombosis of the cerebral vessels may take place in the final stages, and may or may not manifest its presence by special symptoms. Still states that it was noted in 1 per cent. of the autopsies on cases of infantile diarrhea at the Children's Hospital, Great Ormond Street, London. Occasionally an attack of tetany may supervene. Should the drain of fluid from the tissues have been great, the defective circulation in the brain may of itself give rise to many of the above symptoms. Only occasionally must the cerebral symptoms be regarded as of a uremic nature.

Otitis media is to be remembered as a not infrequent complication which may give rise to retraction of the head and symptoms closely resembling meningitis (Still). Any exhausting disease, it would appear, brings with it a special



liability to catarrh of the middle ear, sometimes with external discharge, sometimes without, but in either case adding fresh symptoms to those of the primary disease. Still states that in 79 consecutive autopsies on infants under 2 years pus in one or both ears was found in 32. He thinks it probable that the symptoms described as spurious hydrocephalus may, in some instances, be due to middle-ear inflammation rather than to a toxemia.

Convulsions are always to be regarded as a grave complication, but are not necessarily fatal. Their import is more serious in the later stages of the disease than at the onset.

A true parenchymatous nephritis due to infection would appear to be a rare complication. Kjellberg states he met with it in 47 per cent. of his fatal cases; but competent observers, both English and American, have failed to meet with it, except very occasionally. Fenwick states that albumin in the urine was noted in 17 per cent. of his cases before the fifth day of the disease; but in no instance did the urine show more than a trace. Under the microscope he never observed either blood-corpuscles or epithelial casts. Booker states that necrosis of the epithelium in the convoluted and straight tubules was found in nearly all his cases, and, in not a few, hyaline tube-casts were demonstrable. Infiltration with leucocytes was not seen in any case.

Edema, especially of the extremities, not infrequently makes its appearance about the second or third week of the attack. It is most common in the sub-acute cases, in which the symptoms show a tendency to recur. The edema is generally localized to the back of the hands, feet, and thighs. It sometimes spreads to the face. In a few instances

it is associated with tenderness and then presents a close resemblance to infantile scurvy. Heubner attributes the appearance of edema to a retention of the chlorides and states that it disappears when the infant is fed on a dietary in which the chlorides are greatly reduced. The exact etiology of it, however, is still uncertain.

In a small number of cases purpura may make its appearance in infants in whom much wasting has occurred; it is always to be regarded as a very grave complication, but it is not necessarily fatal.

Purpura is a symptom of infective diarrhea in children which is usually overlooked. Of 100 cases of diarrhea, 11 showed purpura, all of which resulted fatally. All but 2 patients were under 11 months of age. In 8 the eruption was on the abdomen, especially the lower part, and in 4 of these the thorax was also affected. The extremities, where ordinary purpura is more commonly seen, were almost always spared. The purpura was usually a late phenomenon, appearing, on an average, on the thirty-fourth day, one week before the average time of death. It is therefore connected, the author points out, with cachexia rather than acute infection of toxemia. In one patient, however, the rash disappeared and the child improved, but the diarrhea later returned and proved fatal two weeks after the disappearance of the eruption. Transfusion or the administration of horse or other serum could not have been the cause of the purpura, as the latter usually preceded these measures. Nor did the cases suggest any close relation between purpura and the edema which sometimes occurs in children after gastroenteritis. H. D. Rolleston and J. B. Molony (*Proceed. of the Royal Soc. of Med.*, Dec., 1911).

**Diagnosis.**—While there may be, for the first two or three days, some

uncertainty in reference to the character of a diarrhea, a persistent high temperature beyond this period stamps the attack as of an inflammatory nature. After this date fluid evacuations of an offensive odor are characteristic of the toxic form, while small stools passed with much straining and containing mucus and some blood are met with in those cases in which the local inflammatory condition is prominent. Typhoid fever is seldom met with during infancy; its onset is occasionally somewhat abrupt, but after the first few days its course becomes more characteristic. Widal's test should be applied in doubtful cases. Several of the acute specific fevers are sometimes ushered in by an intestinal disturbance, which may, for two or three days, be misleading; of these, scarlet fever and pneumonia are probably the most important.

**Prognosis.**—In infants suffering from chronic dyspeptic troubles, or in those whose nutrition is seriously impaired, the prognosis must always be grave. During the heat of summer an attack of inflammatory diarrhea is of much more serious import than one occurring during the cooler months of the year. In the course of an attack a decrease in the temperature and in the frequency of the stools are favorable symptoms, especially when associated with an improvement of the general appearance, an increase in the amount of urine, and perhaps an increased desire for food. On the other hand, a higher temperature, more frequent and more watery movements, a more anxious expression on the features, sighing and irregular respirations, a feeble and intermittent pulse, suppression of the urine, and the onset of nervous symptoms must all be regarded as of grave significance. In every attack of inflam-

matory diarrhea the prognosis is greatly dependent upon the establishment of correct treatment before the production of serious intestinal lesions.

**Treatment.**—Regarding this disorder as due to an intoxication of the system, either induced suddenly by an absorption from the intestinal tract of toxins in large amount or coming on gradually, owing to the development in the intestinal canal of pathogenic bacteria with a subsequent absorption of toxins, our first efforts should be directed to securing, as promptly and as effectually as possible, the clearing out of the intestinal tract. This we endeavor to effect by means of promptly acting **purgatives**, and by **lavage of the stomach and large intestines**; the small intestines we only reach by means of purgatives.

At the same time the development of bacteria should be checked by withholding food in which they can grow. Milk food, in which we know they develop very rapidly, should be forbidden for many days. Sterile water only should be allowed for the first twenty-four hours. During the early days no astringent drug is to be given to check peristalsis, at this period to be regarded as salutary in character. For the evacuation of the intestinal tract two drugs especially commend themselves on account of their prompt action and of the very slight amount of irritation which they induce. These are **castor oil** and **calomel**. Castor oil is of much value if it can be taken and retained. A full dose, 1 or 2 drams (4 to 8 Gm.), may be given in any convenient way. In many cases, however, there is too great irritability of the stomach for us to attempt the administration of this somewhat nauseous drug, and we can, with advantage, have recourse

to calomel, which acts not only as a purgative, but also, to some extent, as an intestinal antiseptic. It may be given either in one full purgative dose or in a series of small doses, repeated at short intervals. Lesage recommends that if the onset is with high fever, a foul-smelling but not abundant diarrhea, and a considerable amount of tympanites a dose of 1 grain (0.065 Gm.) for an infant under 1 year, and 2 grains (0.13 Gm.) for an infant over that age, should be administered, mixed with a little sugar, in a powder. In those cases where the fever is only moderate, where the abdomen is soft and not distended, and the diarrhea is copious, small doses of  $\frac{1}{10}$  to  $\frac{1}{5}$  of a grain (0.006 to 0.013 Gm.) may be given every half-hour or hour for ten or twelve doses. Other purgatives have been employed, but, in our opinion, they are not so satisfactory.

In a series of 200 cases, the writer found that, in 35 to 40 per cent., **bichloride of mercury**, administered to the nursing mother in doses of  $\frac{1}{32}$  grain (0.002 Gm.) three times a day, had a decided influence upon the gastrointestinal condition and nutrition of the infant. Vomiting, when not due to overfeeding or organic disease, ceased as a rule within twenty-four hours after the treatment was begun; diarrhea was always markedly improved, the frequent, foul-smelling stools containing undigested curds being rapidly replaced by the normal ones. Constipation was in like manner improved by diminishing or increasing the amount of mercury given to the mother. Colic was benefited and the weight was improved in many cases.

This treatment is indicated in any gastrointestinal disturbance of the nursling. It is a harmless procedure even where no benefit results. The effect of the drug upon the non-syphilitic mother is practically nil,

while in the syphilitic mother it improves the general condition. S. V. Haas (Archives of Pediatrics, July, 1912).

Should vomiting be severe and persistent a careful **lavage of the stomach** will often at this period of the disease prove of much value not only because it removes fermenting material and toxins, but because it has a direct sedative action on the gastric mucous membrane. This lavage can easily be accomplished by means of a few feet of rubber tubing to which is attached at one end a soft-rubber catheter (No. 15 or No. 18 English, or No. 30 Charrière), and to the other a small glass funnel. The fluid used may be either sterile water or **normal saline solution**, at a temperature of about 100° F. (37.8° C.). Three or four ounces should be introduced at a time and allowed to escape. This should be repeated until the water returns clear. Occasionally one of the milder antiseptics is added to the solution; we are convinced, however, that the use of them in this way is associated with a definite risk of absorption of an overdose, which more than counterbalances any possible advantage.

Either at the same time or a few hours later when the purgative begins to act, an effort should be made to wash out the colon. The infant should be placed on its back with its hips well elevated, and a **normal saline solution** at a temperature of 98° F. (36.7° C.) be allowed to flow slowly into the intestines through a large-sized rubber catheter introduced for six or eight inches. The pressure in the tube should be slight, the reservoir not being higher than one or two feet above the hips of the patient. If the hips are sufficiently elevated, a little

gentle massage over the region of the sigmoid flexure secures the free passage of the fluid into the descending colon, and then its entrance into the transverse and ascending colon. Should the pyrexia of the infant be high, after the current has been once established the temperature of the water may be lowered to 80° F. (26.7° C.). Lower than this has been recommended by some physicians, but the very interesting experiments of R. Coleman Kemp warned us that we may in this way produce too much depression. The injection should be continued until the water returns clear. If done carefully, the pulse, after the injection, should evince more strength and the general condition of the infant be improved. Afterward a **cool or warm compress**, 70° to 100° F. (21.1° to 37.8° C.), applied over the abdomen and covered with oiled silk and a flannel binder, soothes and assuages pain.

This **lavage of the intestines** may be repeated in six or twelve hours if deemed advisable, and perhaps afterward daily. Bowel washing, in our opinion, however, has been much overdone. With frequent large, watery movements lavage after the first day is unnecessary. Later on in the attack normal saline enemata, given in such a way as to favor absorption, are of much value in supplying sufficient fluid to the tissues and promoting elimination by the skin and kidneys.

Many physicians have advocated at this stage of the disease the administration of drugs which have some action as intestinal antiseptics. Among the more important of these drugs we may mention **resorcin**, **menthol**, **thymol**, **bismuth salicylate**, **sodium salicylate**, **betanaphthol**, and others. It is not

to be forgotten, however, that many of these drugs are very distinct cardiac depressants and renal irritants, and may easily do more harm than good. In our opinion they are better omitted.

Certain intestinal antiseptics, while theoretically powerful, are too irritating to the mucosa to be used in a dose large enough to have any value. Thymol, the naphthol derivatives, and phenyl salicylate, or salol, belong to this class. **Bismuth subsalicylate**, however, is unobjectionable. A comparison of two series of cases, one treated solely by the starvation plan and one treated with the subsalicylate, showed such a decided difference in favor of the drug that it seemed to have undoubted disinfectant properties. Besides the direct disinfectant action of the salicylic radical there is also obtained the sedative action of bismuth itself, which may also be enhanced by giving **bismuth subnitrate** or **subcarbonate** at the same time. A. Hand (Archives of Pediatrics, Feb., 1912).

As regards diet, the author uses barley water and white of egg beaten up with an equal quantity of water, or, better, soda water. H. A. Ellis (Austral. Med. Gaz., Jan. 13, 1912).

The summer diarrheas of children are best classified, according to the writer, as mechanical, proteolytic, fermentative and infectious. The first 2 constitute purely a problem in infant feeding. In the fermentative type, without involvement of the intestinal mucosa, the temperature is apt to be higher, with a decline after 4 or 5 days, while in the infectious type it is not so high but more prolonged. In the former type, the abdomen is commonly distended and the stools green, watery and acid to litmus, while in the latter type, the abdomen is usually flat or sunken, the stools containing pus and blood, and the reaction alkaline. In either type there should be initial purgation with 2 drams to 1 ounce (8 to 30 c.c.) of castor oil. If the oil is not retained, **calomel** should be given in

$\frac{1}{10}$  or  $\frac{1}{8}$  grain (0.006 to 0.012 Gm.) doses every  $\frac{1}{2}$  hour for 10 doses, followed in 3 hours by 2 or 3 teaspoonfuls of **milk of magnesia**. Food should be withheld for 12 to 24 hours, and meanwhile every effort made to supply the proper amount of fluid—2 to 3 ounces (60 to 90 c.c.) per pound of body weight every 24 hours. This should be given as barley water sweetened with saccharin or weak tea. Upon resumption of food the indication in the fermentative type is for a **protein diet**, fats being withheld for weeks afterward, while in the infectious type a **carbohydrate diet** is indicated, with little, if any, fats or proteins. C. M. Pounders (Arch. of Ped., Aug., 1924).

After the intestinal tract has been well cleared of offending material a sedative action on the intestinal tract may be obtained from full doses of one of the **bismuth salts**. The **subcarbonate** or **subnitrate** may be given in 10-grain doses (0.65 Gm.) in an emulsion combined with small doses of an opiate and repeated every three hours till distinct improvement sets in. If vomiting is absent and the stools contain an excess of mucus, small doses of **castor oil** have in our experience proved very serviceable, especially if the pyrexia is still high.

R. *Olei ricini* ..... 3j (8 Gm.).  
*Tinctura opii camphorata* ..... 3j-5iss 4-6 Gm.).  
*Pulveris acaciae*,  
*Pulveris sucrosi*,  
 of each ..... 3ij (8 Gm.).  
*Aqua cinnamomi*,  
 q.s. ad ..... 3iij (90 c.c.).

M. Sig: 3j every three hours for an infant 1 year old.

Under this treatment the pyrexia will be found to subside slowly and the frequency and character of the stools to alter for the better. The castor oil mixture may then be replaced by **bismuth**. Later on one of the newer

preparations of tannin may be added to the bismuth if the movements still continue frequent and watery. A few physicians, however, still prefer the older tannin astringents, *e.g.*, tincture of **kino** or of **catechu**, or the fluidextract of **hematoxylon**. In a few cases the tincture of **coto** has proved useful in our hands.

The value of the administration of **opium** in this disease is a subject on which there has been much difference of opinion. All writers, however, agree that it should be avoided at the onset; it should also not be employed in grave toxemic states with any tendency to drowsiness or stupor, or to cyanosis. Its administration should at once be stopped if under its use the temperature rises, and the bowel movement is unduly checked. But in the great majority of cases, if used cautiously and intelligently, no other drug is so valuable, quieting the motor and sensory systems, relieving pain, and lessening peristaltic activity, thus favoring repair. The preparation employed is immaterial, provided the dose be not too large.

For infants of 3 months:—

*Tr. opii camph.*,  $\mathfrak{m}$ ij-iiij (0.12-0.18 c.c.).

For infants of 6 months:—

*Tr. opii camph.*,  $\mathfrak{m}$ iiij-v (0.18-0.3 c.c.), or  
*Pulv. Doveri*, gr.  $\frac{1}{8}$ - $\frac{1}{6}$  (0.008-0.01 Gm.).

For infants of from 12 months to 2 years:—

*Tr. opii camph.*,  $\mathfrak{m}$ v-viiij (0.3-0.48 c.c.), or  
*Pulv. Doveri*, gr.  $\frac{1}{6}$ - $\frac{1}{4}$  (0.01-0.016 Gm.).

These doses may be repeated every three or four hours, unless the child is sleeping. In apportioning the dose it is wise to consider the size and weight of the infant as well as its age.

If vomiting prevents the administration of the drug by the mouth, **mor-**

**phine** may be given hypodermically in  $\frac{1}{100}$ -grain (0.00065 Gm.) doses to an infant from 8 months to 1 year old, and repeated every six hours if necessary.

Stimulants, in our opinion, are necessary in the majority of cases; they should be used cautiously at first, but liberally in the later stages of the disease. Good **whisky** and **brandy** are preferable to wines, and of these 10 to 15 minims (0.6 to 0.9 c.c.) may be given every two hours. **Aromatic spirit of ammonia** may occasionally be of service in small, frequently repeated doses. **Caffeine** may also be employed, either in solution or in the form of a well-prepared tea or coffee. Where the prostration is severe **strychnine** in  $\frac{1}{100}$ - to  $\frac{1}{200}$ -grain (0.00015 to 0.000 Gm.) doses, given hypodermically, is of service. **Atropine**,  $\frac{1}{1000}$  grain (0.000065 Gm.), hypodermically, is recommended by la Fetra. **Camphor** dissolved in oil has also proved serviceable.

In all instances where the temperature runs an elevated course we have much confidence in the value of **hydrotherapy**. This treatment may be employed in the form of tepid sponging, **cool baths**, the **cold wet pack**, or **cool irritation of the intestines**. Of the three methods our preference is for **tepid sponging** or cool baths. Whenever the temperature of the body rises above 104° F. (40° C.) the infant should be sponged with water at 85° F., or placed in a bath containing water at a temperature of 90° F. (32.2° C.), and remain in it from three to five minutes, the duration varying according to the age and feebleness of the infant. It is to be remembered that infants are affected by a cold bath more promptly than

adults, and are more easily depressed by it. Care should be taken, therefore, to watch its effects, and, if necessary, to use stimulants after it is over.

A **cold pack** may occasionally, with advantage, replace the cool bath where circumstances are not convenient for the employment of the latter. Of late years the irrigation of the colon with cool **normal salt solution** has been employed in cases of hyperpyrexia. It is unquestionably a more powerful method than either bath or pack, and, when used with discretion, may prove of more value. Its action, however, is less under the control of the physician than that of baths, and serious depression of the nerve-centers may result from the employment of too cold and too long continued irrigation.

Should the prostration become extreme and hydrencephaloid symptoms make their appearance, subcutaneous injections of a sterilized **normal saline solution**, as described in the article on cholera infantum, ought to be employed. In severe cases two injections a day of 50 c.c. ( $1\frac{2}{3}$  ounces) each should be given. Not only do these injections stimulate the flagging circulation, but they dilute the toxins in the blood and favor their elimination through the excretory organs; in many instances they check, in a remarkable way, the symptoms of nervous irritation.

**Careful feeding** and **intestinal irrigations** with boiled water, 0.02 per cent. **boric acid** or **naphthol solution**, or, better, **normal saline solution** are indicated. During irrigation the child should be upon its right side; a soft-rubber catheter should be used and the receptacle of the fountain syringe through which the lavage is given should be elevated not more than five or six inches above the patient. The

quantity employed should be from 1 pint to 1 quart and the fluid should be cold if the patient's temperature is elevated, hot if the latter is subnormal. Perrot (*La quinzaine thérap.*; *Amer. Jour. Med. Sci.*, Aug., 1907).

The treatment of diarrhea due to alimentary intoxication consists in combating the collapse, cutting short the intoxication, and slowly bringing the child back to a diet commensurate with its caloric requirements. The first indication may be met by hypodermoclysis of **saline solution**, using 50 to 100 c.c. (1½ to 3¼ ounces), and repeating as is deemed necessary. The second indication is met by withdrawing the food entirely and allowing water only for twenty-four hours. With the subsidence of all symptoms, begin feeding as follows: As exceedingly small quantities of fat are injurious, begin with **centrifugated breast milk**, if possible, given in teaspoonful doses five times a day, or an equal quantity of **buttermilk**, to which neither sugar nor meal has been added; or, if this is not at hand, fat-free milk may be used. As a diluent, and to supply the liquid necessary, water and a thin cereal gruel may be used or given separately. After an interval of twenty-four hours, provided treatment has been well tolerated, without any evidence of return of the intoxication, the separate quantities of milk may be increased to 2 teaspoonfuls, which after two or three days may, under the circumstances mentioned, be doubled, and so on, until they are gradually brought to a **diet** (free of fat in artificially fed infants) that will temporarily meet their needs from a caloric standpoint, having added, in the mean time, with their increased tolerance of the buttermilk (where employed), 30 Gm. (1 ounce) of sugar, preferably maltose, and 15 Gm. (½ ounce) of flour to each liter (quart) of buttermilk while boiling. The child should not be kept on the buttermilk diet longer than six weeks. After this time whole-milk dilutions will be necessary to meet its needs. In case the infant was at the breast,

after four or five days of careful feeding with centrifugated breast milk, it may be returned to the breast, the amount of milk being carefully controlled. Butler (*Jour. Amer. Med. Assoc.*, April 4, 1908).

Opinion of a committee of the Academy of Medicine concerning Quinton's "marine plasma:" It consists of **sea water** collected under aseptic conditions and rendered isotonic by the addition of sterile water. It has sometimes given good results when, as the result of profuse diarrhea, the fluid content of the organism has been greatly reduced, but since ordinary physiological salt solution gives analogous results in the same case, the former cannot be considered either as a specific or panacea in infantile diarrhea. Wurtz (*Bull. de l'Acad. de Méd.*, May 14, 1912).

Treatment of infantile gastroenteritis by subcutaneous injection of "marine plasma," i.e., sterilized **sea water**. The writers give milk at once with the injections, and regard the strengthening from the milk as an integral part of the treatment; the children are transformed by the injections so that they are able to take care of the milk. Between their feedings they are given a bottle of water or it is fed to them with a spoon, giving as much water as the child will take readily. The amounts of sea water to be injected vary with the nature of the trouble. With enteritis causing constipation, they inject from 10 to 30 c.c. (½ to 1 ounce) twice a week, feeding the child with from one-eighth to one-sixth of its weight. With athrepsia and ordinary diarrhea, they inject from 30 to 100 c.c. (1 to 3½ ounces) two or three times a week, and feed from one-seventh to one-fifth of the weight. Almost moribund children recover under this regimen. They published in 1905 a series of experiments including 2592 days of tests to determine the superiority of sea water over ordinary salt solution for these injections in infants. They found that the infants increased in weight twice as fast under the sea water. This increase was not due to

the weight of the sea water, as the increase in weight was out of all proportion to the amount of sea water ingested. O. Macé and R. Quinton (Revue mens. de Gynéc., d'Obstét. et de Péd., June, 1912).

The writer considers infantile diarrhea under 3 headings: (1) *Mechanical*, due to undigested pieces of food, fruit-skins, seeds, etc. The treatment is **castor oil** or **calomel**, **rest in bed**, **barley water** or other gruel for 12 hours, plenty of **water**, and then a bland diet of **cereal** and **boiled skimmed milk**. (2) *Fermentative*. In mild **sugar** fermentation, no **purge** is needed until there is fever. All sugars should be omitted and the **milk modification** **boiled** for 3 minutes, with 1 teaspoonful of **compound chalk mixture** added to each bottle. In more severe forms, he uses **albumin milk**, **skimmed milk** with powdered **casein**, or **lactic acid milk**. A **purge** is used only in early cases with fever not yet emptied by diarrhea. Other useful measures are **colon irrigation** at the onset, **water** freely, **sodium bicarbonate** by mouth, skin or vein when air hunger develops, **compound chalk mixture** (better than bismuth), often **brandy** and **caffeine**, and **opium** if necessary. In the less common *protein* form of fermentation, the stools are brown and foul, instead of green and acid-smelling; a **low protein** and fairly **high carbohydrate diet** is used. (3) *Infectious*, with actual invasion of the mucosa by bacteria, most commonly dysentery bacilli taken in *per os*; probably the streptococcus and *B. aerogenes capsulatus* are also causative. Treatment is the same as in (2), except as to diet. The dysentery and streptococcus cases receive a **low protein** and **high carbohydrate diet**, while the gas bacillus cases are fed on a **lactic acid milk** with **low sugar diet**. Hill (Jour. Amer. Med. Assoc., lxxii, 1653, 1919).

In summer diarrhea the writer gives **castor oil** and **calomel** in divided doses followed by **calcined magnesia** or **milk of magnesia**, with temporary starvation at first. If this fails, **bismuth subcarbonate** or **subgallate** may be given for a

short period, or 1-dram (4 c.c.) doses of **chalk mixture** every 2 hours. Castor oil should not be given late, nor repeated. **Paregoric**, **Dover's powder**, or the **tincture of opium** should be used for excessive peristalsis and pain unless the bowel is already well emptied, or there are infrequent, foul stools, or in early acute cases with fever, cerebral symptoms and scanty elimination. In marked tenesmus 5 to 10 drops of **opium tincture** in 1 ounce (30 c.c.) of starch water as enema usually suffices. Among the stimulants, **atropine** hypodermically is especially useful in hypothermia. **Anointing with oil**, **wrapping in cotton**, and **hot water bags** are serviceable. To prevent acidosis, carefully prepared **sodium bicarbonate** should be given in 15 grain (1 Gm.) doses every 3 hours, in all but the mild cases. J. F. Sinclair (N. Y. Med. Jour., Aug. 3, 1921).

The author discusses **intravenous** use, in *dehydration*, of **normal salt solution**, 5 per cent. **glucose**, 3 per cent. **sodium bicarbonate**, or **glucose-acacia solution** injected at 110° F. by gravity into the longitudinal sinus, at the rate of 3 or 4 c.c. a minute, after shaving the scalp closely and under strictest asepsis. Donnelly (N. Y. Med. Jour., Aug. 3, 1921).

The writers have called attention to the value of **intrapерitoneal injections of salt solution** in cases with dehydration. They find peritoneal puncture safe provided the bladder is empty, distention not extreme, and rigid asepsis observed. The amount should never exceed 300 c.c. (10 ounces) and in infants below 4000 Gm., repetition of 150 c.c. is safer. Water given through a nasal tube will sometimes prevent dehydration. Gittings and Donnelly (Amer. Jour. Dis. of Childr., Feb., 1922).

**Dietary.**—For the first twelve or twenty-four hours, according to the severity of the case, only cool sterile water should be permitted to the infant. After this period a weak sugar-of-milk solution may be given in small quantities to infants under 3



months, and to those over 3 months thin barley or rice water with sugar of milk may be allowed. Great caution must be exercised with all albuminous foods so long as the stools retain their offensive odor. White of egg, or albumin water, forms an excellent method of administering an easily assimilated protein. To prepare it, the white of an egg is to be shaken up in a flask with 8 ounces (240 c.c.) of water; the solution is then to be strained through muslin, and a little salt and sugar of milk added.

Weill, Lumière, and Péhu found a 10 per cent. solution of sterilized **gelatin** in physiological saline made into a jelly and kept in a closed tube effective. Before each feeding the solution is melted on a water bath and 10 c.c. ( $\frac{1}{4}$  ounce) of it are poured into the bottle containing the milk. At the fourth or fifth stool after the beginning of the treatment, the feces show marked improvement, the odor disappearing and the color and consistence approximating the normal. The gelatin facilitates digestion of the milk by causing the clots to break up into fine particles, and as a result the stools are rendered more solid in consistence. The measure gives especially good results in light forms of diarrhea. The necessity of stopping milk entirely may thus be avoided. Similarly, when feeding with milk is resumed, after suspending it for a time in the more pronounced cases, the use of gelatin is indicated. The writer found this treatment very useful excepting in severe diarrheas of choleraic type, gelatin having no power to counteract the infectious process. Lereboullet (Paris méd., Dec. 2, 1911).

The writer uses in alimentary intoxication of infants an **intravenous infusion** of 280 to 300 c.c. of a 10 per cent. solution of **glucose** preceded by 1 unit of **insulin** for each gram of sugar. Priesel and Wagner (Klin. Woch., Mar. 12, 1925).

A carefully prepared whey may also be allowed, and is often relished. In older children a weak broth with barley or rice, or one of the peptonized foods, may be administered with advantage. Milk in all forms should be forbidden in the early acute stage; only when the pyrexia has, in great measure, subsided, and the stools have begun to assume a more normal appearance, may a weak dilution of a comparatively fat-free milk be allowed; the strength of this dilution should be only gradually increased.

As soon as the diarrhea begins, **castor oil** should be administered and food should be withheld for at least twelve hours. During this period water should be given frequently, by mouth if there is no vomiting, by rectum if vomiting is present. The best treatment for the vomiting is **lavage and starvation**. If the infant presents symptoms of marked loss of fluid, such as a dry, loose skin, parched tongue, depressed fontanel, and sunken eyes, **salt** should be added to the water, so that a **hypotonic solution** of 0.3 or 0.4 per cent. is given. If we make use of a normal solution edema is apt to ensue. Fever should be controlled by means of occasional **baths** at 85° F. (29.4° C.) and frequent **packs** at this temperature or lower, if necessary. There is no medicine, except, perhaps, a stimulant in case of collapse or severe prostration, which has any value; bismuth, the astringents, and the opiates are ineffectual. One of the fundamental principles of the feeding is that it should be begun in very small quantities, a teaspoonful every two or three hours. Another rule is that fats and sugars should be avoided. We must not forget, however, that the various food constituents differ in their action according to their correlation. Sugars when given with dextrin or starches lose their laxative effect. The same is true for both fats and sugars in combination with proteins. It is due to these considerations that we can

begin with the feeding of the "**casein milk**" of Finkelstein, a food containing a high percentage of proteid, a moderate amount of fat, and but little sugar and salt. If we have not this food at our disposal, skimmed milk may be given in small doses. Hess (Jour. Amer. Med. Assoc., July 15, 1911).

Underfed, poorly nourished infants with diarrhea, do best on the **milk and water** mixture, boiled, without sugar. Bad diarrheas, or those that do not improve upon these mixtures are benefited by **albumin milk**. Infants that have had repeated or prolonged attacks of diarrheas do best upon *Eiweiss Milch*. Older, well-nourished infants with a diarrhea do best upon a **barley-gruel** diet for a few days. Infectious diarrhea, if seen early, should have a **cathartic** and **starvation** for forty-eight hours and no longer. The milk-and-water mixtures, boiled, or *Eiweiss Milch* (**albumin milk**) should then be given. Cathartics should be given to infants with diarrhea with great discretion. Dennett (Med. Rec., Dec. 2, 1911).

Report of results obtained in summer diarrhea with **albumin milk** according to Finkelstein and Meyer. This is prepared as follows: A tablespoonful of essence of rennet (or 2 tablets of rennet) is added to 1 liter (quart) of milk, which is then placed in a water bath at 42° C. (107.6° F.) for one-half hour. It is then filtered slowly by gravity without any pressure for about an hour, through cheesecloth. The coagulum is then washed twice in half a liter (1 pint) of water through a very fine sieve and forced through by means of a wooden club. Then half a liter (1 pint) of buttermilk is added. This mixture was given for from two to fourteen days, in quantities corresponding to the usual feeding mixtures prescribed for the respective age. In the series of 42 cases, 20 of which belonged to a very severe type of the disease, there were 9 deaths, a mortality of 21 per cent. Excluding 4 of the cases in which the children

were practically moribund when admitted, there were 5 deaths, a mortality of 13 per cent. The special indication for this mixture is found in those cases in which marked emaciation has taken place owing to undue prolongation of restricted diet. Heiman (Amer. Jour. of Obstet., Aug., 1912).

The writer used **casein** or **albumin milk** in 175 cases of gastroenteritis in infants. Of these 110 were dyspepsia, 8 toxic enterocatarrh, 40 enterocolitis, and 17 decomposition (Finkelstein nomenclature). There were only 12 deaths among all these cases, which could not have been averted with any other feeding. Four of these patients were brought into the hospital moribund and 4 had bronchopneumonia; of the other 4 deaths 1 was a case of toxic enterocatarrh, and 3 were very severe decomposition. According to the writer's observations fourteen days of casein feeding suffices in most cases (Finkelstein and Meyer recommend from six to ten weeks). Casein milk offers the best method of treatment of diarrhea in infants. Beck (Jahrbuch f. Kinderheilkunde, March, 1912).

Notwithstanding the extreme heat of 1911, the epidemic of summer diarrhea was comparatively benign, only 100 of the infants dying during the month of August, although there were over 3000 sick. The writer had in the hospital 58 exceptionally severe cases, but only 6 of the infants died, a mortality of 10 per cent. This favorable outcome was due to his method of feeding the infants. Nothing but water was allowed until the alarming symptoms had subsided, the coma, collapse, high fever and albuminuria; this generally took from one to three days. Then he gave the infant the ordinary milk mixture, but without the usual 2 per cent. of cane-sugar, diluting the milk with 4 parts water, then with 3 parts, and then 2 parts. This was generally borne by the end of the first day, and he kept this up until all signs of intoxication had disappeared and the infant was

ready to drink spontaneously. Then he returned to the sugar, 1 part milk to 2 parts barley water. The diluted milk without sugar seemed to answer the same purpose as "albumin milk" of Finkelstein and Meyer. C. E. Bloch (*Ugeskrift f. Laeger*, July 4, 1912).

During the past few years the value of **buttermilk**, either raw or pasteurized, has been emphasized by many clinicians. Buttermilk contains very little fat, a moderate amount of sugar, and a considerable amount of digestible proteid in the form of lactate of casein. It is distinctly acid, owing to the presence of lactic acid, and in the raw state is swarming with lactic acid bacteria. The lactic acid and the lactic acid bacteria have an inhibiting action on the development of other forms of bacteria.

No better basis for an artificial food for children in the first year of life exists than **buttermilk**; further, in cases of gastrointestinal disorders in infants, with the passage of fluid, partially digested stools, its use as a diet is attended in most cases with excellent results. Frequently within two or three days the diarrhea ceases, firm normal stools are passed, and the child begins to increase in weight. It is important that the buttermilk should be derived from the cream of perfectly fresh whole milk. A food prepared by adding 1 ounce (30 Gm.) of wheaten flour and 1½ ounces (45 Gm.) of cane-sugar to every 2 pints (1 liter) of buttermilk, the whole being boiled, with stirring, for two minutes, recommended. Quantities varying from ½ pint (¼ liter) to 2 pints (1 liter) were given daily, and although the children did not like it at first they soon took it well. In a few cases it was found unsuitable and a more fatty diet resorted to. The infant mortality in the Kaiser and Kaiserin Friedrich Hospital in Berlin has fallen since the use of this food. The good results are due chiefly to

the presence of the casein in a finely divided form, and the writer does not think the diminished fat content of great importance, though most writers consider this factor also of value to feeble digestion. Caro (*Arch. f. Kinderheilk.*, Sept., 1902).

Infants with severe gastrointestinal troubles improved to a remarkable extent when put on **buttermilk**. In 22 cases of acute gastroenteritis, including 8 very severe ones, all the children recovered rapidly, as also 3 adults with mucomembranous enterocolitis and a large number of children with chronic gastrointestinal troubles. The toxi-infectious symptoms vanished in the acute cases in less than twenty-four hours. Decherf (*Semaine méd.*, vol. xxiv, No. 44, 1904).

All infants do not do equally well with the same nourishment. Even under the same mixture of cows' milk, it often happens that one child will do very well, while another will be very constipated, and still another infant will have very loose stools. The reason for this is explained by the congenital variance of different infants. Constipation in infants can usually be cured by the addition of one or two carbohydrates. Diarrhea, on the other hand, is more difficult to cure. The writer used **buttermilk** in cases of diarrhea with very good results. It contained about 1.4 to 1.7 per cent. of fat. Instead of adding sugars to the buttermilk, he added flour, about 50 Gm. (1½ ounces) to the quart (liter). This buttermilk differs from that commonly used in having a higher proportion of fat and also in having very little sugar, which, it is well known, causes diarrhea. In mild cases of diarrhea substituting this buttermilk feeding for one or two of the regular feedings often has the desired result. Karl Stotte (*Monats. f. Kinderheilkunde*, June, 1912).

In most instances the infant is apt to object to its taste, but this is improved by the addition of a cereal gruel and 5 grains (0.3 Gm.) of cane-

sugar to the ounce of buttermilk. The whole may then be pasteurized, if desired. Morse states that he has obtained better results in the treatment of diarrheal cases from pasteurized buttermilk than from any other milk preparation.

The use of the **lactic acid bacillus**, chief among which is the *Bacillus bulgaricus*, has also been praised by various writers.

The writer advises that the clear fluid from Bulgarian buttermilk be used as the culture medium for injection. The following are his directions: Take 500 c.c. (1 pint) of pure milk, remove the cream, add 10 Gm. (2½ drams) of cane-sugar, and boil for a quarter of an hour; cool to 42° C. (107.6° F.) and add 1 tablet of the **lactobacilli**, crushed. Keep for ten hours in a water bath at 42° C. (107.6° F.), when the buttermilk will be formed thick and creamy. Place in a refrigerator until a fluid separates, and siphon off the clear fluid from the bottom. This fluid is rich in bacilli, sugar, and peptones, and is ready for use in the manner suggested. Even though further trials prove its efficacy, the trouble involved in its preparation will be a serious deterrent to its use in private practice, although there should be no difficulty at institutions with a bacteriological laboratory. W. H. Walsh (The Hospital, Dec. 5, 1908).

The bacterial diarrheas of infants may be classified into parasitic and saprophytic, the former of which must be combated by serotherapy and vaccine while the latter require other methods, one of which is specially taken up by the writer, namely, the antagonism of the lactic acid bacteria to the fermentation conditions in the intestine. His investigations on this subject were prompted by the work of Tissier in the Pasteur Institute in Paris, who found that the predominating organism in the healthy infantile intestine is *Bacillus bifidus*, while in disease other forms

appear. Among these latter Tissier found only one, *B. perfringens*, that was pathogenic to animals, which attacks protein substances and their derivatives. It is a large rod with square ends, staining by Gram's method; is anaërobic, ferments sugar and has the special property of causing solution of meat or the white of egg in sealed tubes. Tissier believes this organism to be the cause of fermental diarrhea. As predisposing causes, he believes that lack of digestive power and unsuitable food play the chief part. The indications for treatment he thinks are removing the fermenting intestinal contents by purgation and restoring the normal intestinal flora. The increase of carbohydrates in the food will favor the latter, but the more specific treatment is to introduce into the intestines an organism capable of inhibiting the growth of the abnormal forms, which he found most conveniently in the lactic acid bacillus. Taking up these ideas of Tissier, the writer began his work on the subject in the autumn of 1905 and has continued it since then. **Buttermilk**, containing large numbers of lactic acid bacilli, seemed to him to combine both food and medicine. The selected buttermilk was first pasteurized to kill all other organisms and then inoculated with a pure culture of lactic acid bacilli and ripened until the development of the organism had brought about the proper acidity and precipitation of the casein. In the majority of cases the buttermilk was used only after other measures had failed. After a dose of **castor oil** or **calomel** to empty the bowel nothing but boiled water was given for twenty-four hours and only barley water for another twenty-four, then a weak milk modification was used, gradually strengthened as improvement appeared. In the first 35 cases tried with the **lactic acid** treatment, 5 were not strictly fermental cases, but were selected for experiment, and in these no improvement was seen. In 23 there was a rapid change in the character of the dejecta

and gain in weight. In 3 cases the diarrhea ceased without gain in weight and in 9, including those mentioned above, there was no improvement. Only 2 of the cases of total failure were frankly fermental cases, 2 were dysenteric. The use of non-pasteurized buttermilk was tried in 14 resistant cases after pasteurized milk had failed, and in these cases immediate improvement followed its use, which he attributes to the introduction of large numbers of living lactic acid bacilli into the intestine. The results were so favorable that he concluded to adopt this treatment as a routine, and he has thus treated several hundred cases of which he has fairly complete records of 120. Not all of the babies received unpasteurized buttermilk; some were treated with various formulas of modified milk similarly ripened. In all of these that were truly fermental diarrheas, numbering 100, the treatment was successful in 74, partly successful in 12, and failed in 14. There are occasionally cases in which buttermilk does not seem adapted to the child's digestion, and these were treated by only continuing it until the alteration of the movements had occurred, as a temporary weapon against the saprophytic infection. The attempt to use modified milk, similarly ripened, was not a complete success, and he was compelled to confine his work to formulas containing no fat. There is also a difference in the effects of different strains of lactic acid bacilli, and he is still experimenting as to this point. His general conclusion is, however, that in this treatment we have a very valuable weapon for combating fermental conditions, and that it should be used in every case of this type. C. H. Dunn (Jour. Amer. Med. Assoc., Aug. 21, 1909).

*Bacillus bulgaricus* was used by the writer with marked benefit, all cases except the most advanced being cured. After preliminary dose or two of castor oil, liquid cultures were given in doses of  $\frac{1}{2}$  or 1 teaspoonful

every three or six hours, in a little water with milk-sugar. Diet for first one or two days: Whey from pure milk, diluted according to age; later, add milk in increasing amount, and for older babies barley or other cereal water. Harrington (N. Y. State Jour. of Med., Feb., 1912).

Looking upon *infantile enterocolitis* as due to heightened pathogenicity of the colon bacillus, the writer used a **polyvalent stock colon bacillus vaccine** in 46 mild cases, giving 100 million killed germs in the buttock every 3 days. He considers the results encouraging. Spolverini (Riv. di clin. ped., Mar., 1921).

**Hygiene.**—During the attack the infant should, as far as possible, be confined to its cot. Soft, unirritating flannel should be worn over the abdomen to afford some protection against sudden changes of temperature in the external air. Great care should be exercised lest the buttocks become irritated by the discharges; diapers should be changed promptly as soon as soiled, and the application of some greasy emollient will frequently prevent the development of the erythematous and sometimes ulcerative condition which in these cases is so liable to occur.

The infant, of course, should be allowed all the fresh air possible. The room in which the infant is kept should be light and well ventilated, and an effort should be made to maintain its temperature between 65° and 68° F. This in midsummer in cities is well-nigh impossible. But sometimes much can be done by keeping the patient on the shaded side of a veranda or in a tent on a lawn. Electric fans keep the air moving and encourage evaporation on days extremely oppressive. As soon as the violence of the attack has passed off, the infant should be sent, if practicable, either to the seaside or to a bracing country or mountain air.

**INFLAMMATORY DIARRHEA**  
 in which, in Addition to the Systemic Infection, the symptoms of an Acute Local Inflammation Have a Prominent Part.—**ACUTE ILEOCOLITIS; DYSENTERY.**

Under the term ileocolitis, or dysentery, several forms of inflammatory diarrhea have been described. In the cases most frequently met with the symptoms are chiefly catarrhal; in a few the intensity of the inflammation leads to a necrosis of the superficial tissues and the formation of a pseudo-membrane, and in a third class an ulceration of the lymph-nodes and tissues surrounding them is the chief characteristic. These divisions, however, are as a rule more easily made by the pathologist than by the clinician.

Inflammatory diarrhea is more frequently met with in the later than during the earlier weeks of summer, and may occasionally appear as a limited epidemic. For the special etiology and morbid anatomy we must refer the reader to what we have already said at the beginning of this article.

In 29 cases of infectious summer diarrhea, 18 proved to be due to *Bacillus dysenteriae*, of the Hiss-Russell type in 16 and the Flexner type in 2. The procedure advocated is to make cultures as soon as the stool is obtained. A little mucus is washed in sterile saline and 2 plates of Endo medium inoculated. After 18 hours' incubation the white colonies are picked and transferred to glucose agar. If not gas-producing, the organisms are cultured on triple sugar media and a tube of plain broth inoculated to determine motility. If the organism proves to be Gram-negative, non-motile, and produces a red butt and colorless slant on triple sugar media, it is classed as belonging to the dysentery group. In stools obtained before the fourth day of the disease, the picture seen in direct

smears was almost typical and could be of diagnostic service. S. G. Graham (Canad. Med. Assoc. Jour., Aug., 1921).

**Symptoms.**—The symptoms in this form of the disease generally commence abruptly, and for the first few days closely resemble those of the preceding form. The vomiting, however, is not so persistent; the temperature, although high at the onset, soon falls, and remains about 103° F., and the motions are fluid, of a greenish or greenish-yellow color, and frequent, gradually becoming less in amount. They are passed with considerable abdominal pain and rectal straining, and contain much mucus and a variable amount of blood. Their color changes to brown or greenish-brown, and their odor becomes offensive. Under the microscope undigested material, epithelial cells, pus-corpuscles, and streptococci, with other forms of bacteria, are seen.

The writer calls attention to the sudden onset with fever, anorexia, irritability, and vomiting in the dysenteric cases. R. C. Spence (So. Med. Jour., Mar., 1922).

The abdomen may show signs of distention; tenderness on pressure may be elicited along the course of the colon, and the urine, if collected, may show the presence of a small amount of albumin. As the disease progresses the severe straining frequently leads to a troublesome prolapse of the bowel.

If proper measures are employed, the severity of the symptoms generally subsides toward the end of the first week. The motions diminish in frequency; they no longer show signs of blood; pain and tenesmus lessen, and the mucus decreases in amount. Recovery, however, is apt to be slow, and, for some time, relapses on the slightest indiscretion are liable to take place. The per-

sistence for several weeks of brown mucous stools, with moderate pyrexia and a failing nutrition, are, according to Holt, an indication that ulceration has taken place. In the more severe form the temperature remains steadily high; the motions are very frequent and contain much blood, and the infant quickly falls into a typhoidal state, in which stupor, delirium, or convulsions are liable to occur. If the case survive, the symptoms may moderate; but prostration is extreme, and some pulmonary or cerebral complication is apt to turn the scale on the wrong side. More or less ulceration is always present in these cases, rendering recovery particularly slow. A long period, during which careful dietetic and medicinal measures must be faithfully employed, is required before complete restoration to health can be secured.

The membranous type of the disease is, fortunately, of rare occurrence. In this form the symptoms are of an alarming character from the very outset. Not only do the stools contain much blood and mucus, but an examination of them under water may reveal numerous shreds and sometimes large patches of pseudomembrane. Pronounced nervous symptoms, such as stupor or convulsions, may at the onset mask the symptoms of local inflammation. Such cases generally run a severe course, typhoidal symptoms develop early, and recovery is comparatively rare.

Occasionally we meet with cases which, for the first two or three weeks, have shown symptoms of gastroenteric infection rather than of local inflammation, and in which, owing to the feeble constitution of the infant and to the intensity of the local irritation, a follicular ulceration develops and symp-

toms of local inflammation make their appearance. The motions become slimy and show traces of blood; their color is, most frequently, a dark green or brown, and their odor offensive. Pain at this stage, though present, is no longer so prominent a feature as during the earlier stages of the disease; pyrexia is only moderate; the motions are not very frequent, but the strength of the infant gradually fails, and general emaciation becomes very noticeable. Under the microscope the stools are seen to contain epithelial cells in large numbers, numerous leucocytes, and streptococci associated with bacilli.

The course of these cases is generally downward. The disease assumes a chronic character. Exacerbations and relapses are easily excited. Only the few recover completely, and in these convalescence is always slow. The fatal result is frequently hastened by some intercurrent disease.

**Diagnosis.**—Great care must be taken to differentiate this form of diarrhea from intussusception, as in the case of the latter disease much valuable time may be lost. In the early stages of intussusception we have no pyrexia. Vomiting is an initial symptom, and is followed by recurring colicky pains with straining. This group of symptoms should always put us on our guard, especially if blood-stained mucus is passed almost free from fecal matter. Careful palpation of the abdomen should be made to elicit any signs of tumor. Should any rigidity of the abdominal wall interfere with effective palpation, it is often advisable to procure complete relaxation by means of a little chloroform. Typhoid fever, as we have before mentioned, very rarely presents itself in an infant. Severe membranous diarrhea may be confounded with

meningitis at the onset, but the course of the disease will make the diagnosis easy.

A careful study of the autopsy records and clinical histories of 100 fatal cases of infantile diarrhea occurring in a series of years at the Thomas Wilson Sanitarium, Baltimore, brought out the following facts: "1. Mucus is evident to the naked eye in a large percentage of diarrheal stools of infancy. Its absence renders the presence of serious intestinal lesion improbable. Mucus in large amounts may be found in the stools in all intestinal disorders, but the proportion of cases with extensive intestinal alteration is greater when the quantity of mucus is in considerable excess. 2. The appearance of blood in the diarrheal dejecta of infants suggests an alteration of the intestinal mucosa in proportion to the amount of blood present. On the other hand, extensive changes may occur in the bowel wall without the macroscopic presence of blood in the discharges. 3. In like manner, the presence of pus in the diarrheal stools of infants indicates, according to its quantity, alteration in the mucosa, particularly that of the large bowel. The failure, however, to detect pus in the stools with the naked eye does not preclude the possibility of extensive intestinal lesion. 4. Blood and pus are more frequently found in diarrheal movements in the middle half of infancy, and these elements at this time form a correspondingly more reliable index of the conditions of the intestinal mucosa. 5. Blood and pus rarely appear in the diarrheal discharges of infants before the beginning of the second week of their illness. They are more frequently found from the third to the sixth or eighth week, and are usually absent after this period, when, if the baby survives, the condition may assume a marantic character. 6. Blood and pus are often found mingled in the same stool. Less often blood appears alone, and still less frequently is pus noted in the dejecta of infants who have not

passed blood. The presence of these elements indicates the probability of thickening and infiltration or of ulceration of the mucosa of the small, but more certainly of the large intestine." J. H. M. Knox (Jour. Amer. Med. Assoc., Oct. 17, 1908).

A diagnosis of the presence of ulceration is to be made from the whole character of the case and its history, rather than from any one special symptom. When mucous stools persist for several weeks with only moderate fever, but with rapid wasting and loss of strength, a condition of ulceration is more than probable.

Case of ileocolitis in a boy of 3 years complicated by the presence of tapeworm. The boy was taken violently ill with all the symptoms of ileocolitis, which persisted for about three days, then gradually subsided, the treatment having consisted of colonic irrigations and a carefully regulated diet. Ten days later sections of the *Tania saginata* were found in the stools, and later the boy again became violently ill. Being in an extremely weakened condition measures were employed to build him up as rapidly as possible. Tonics were used, good substantial food given, and the seashore recommended. Four attempts were made at various intervals for the removal of the tapeworm, the entire worm being finally passed ten months after its discovery. M. Ostheimer and H. A. Spangler (Penna. Med. Jour., Sept., 1908).

**Prognosis.**—The prognosis must be greatly dependent on the vitality and strength of the infant, upon the hygienic and dietetic conditions that can be secured, upon the severity of the attack, and upon the season of the year. Delicate infants under unhygienic conditions generally succumb early. Continuous high fever, the presence of a large amount of blood in the evacuations, severe nervous disturbance, and



symptoms indicative of extreme feebleness of the circulation are always to be regarded as unfavorable.

**Treatment.**—The same measures are to be employed at the outset in this group of cases as in the preceding. Milk and all milk foods are to be forbidden. A full dose of **castor oil** or an effective dose of **calomel** is to be promptly administered, and followed within a few hours by copious irrigations of the colon with tepid **normal saline solution**. A **compress** over the **stomach**, to which we have already referred, should be applied. After complete irrigation of the intestines, should painful straining persist, a small quantity (5j to 5ij—4 to 8 Gm.) of a thin **starch solution**, to which from 1 to 3 drops (0.06 to 0.18 c.c.) of **tincture of opium**, according to the age of the infant, has been added, should be gently thrown into the rectum, with the object of moderating excessive peristalsis and lessening tenesmus. These opiate injections may be repeated every four hours, watching their effects carefully. Should the stools contain a large amount of blood, rectal injections of **hot normal saline solution**, 106° F. (41.1° C.), to which a small amount (5j to 5ij to Oj—4 to 8 c.c. to 30 c.c.) of solution of **adrenalin**, 1 to 1000, has been added, may be slowly administered, allowing the fluid to escape without hindrance. Fluidextract of **hamamelis** (5iv to Oj—16 to 30 c.c.), **tannic acid** (gr. xxx to lx to Oj—2 to 4 c.c. to 30 c.c.), and weak **nitrate of silver** (1:2000) solutions have all been recommended for use in this acute stage. We consider them of more advantage after the acute symptoms have subsided.

**Yeast** has been found a very satisfactory remedy in various cases of

gastrointestinal affections in children at the Strassburg polyclinic. The benefit was particularly striking in enteritis accompanied by much putrefaction in the intestines. The yeast preparations alone triumphed in several very severe cases that had not responded favorably to calomel, bismuth, or lavage of the intestines. In other cases the ordinary measures seemed to do no good until reinforced by the yeast. Sittler (Münch. med. Woch., Bd. liii, Nu. 36, 1906).

Internally, during the acute stage, we place most reliance on an emulsion containing **castor oil**, in from 3- to 5-minim (0.18 to 0.3 c.c.) doses, associated with **Dover's powder** or **paregoric** (*vide* treatment gastroenteritis), and given at intervals of three or four hours. This emulsion should be made palatable. After the acute symptoms subside, one of the insoluble preparations of **bismuth**, to which we have before referred, should be given in full doses, suspended in a mucilage with some aromatic water. More powerful astringents are only permissible in the later stages. **Opium** in doses sufficient to relieve pain and restlessness is, in our opinion, of distinct service. Stimulants are required in the majority of cases. Old **brandy** or **whisky** forms one of the best, and, given well diluted in a little sweetened or albumin water, is acceptable even to the youngest infant.

This mixture is useful when dietary restrictions are unnecessary:—

**R. Gambir**

(catechu)	2.0	Gm. (30 grains).
Tinctura cinna-		
moni ...	10.0	Gm. (2½ drams).
Benzosul-		
phinidi ..	0.925	Gm. (15 grains).
Aqua des-		
tillatae ...	90.0	Gm. (3 ounces).

M. Sig.: One teaspoonful every half hour. R. Fischl (Nouveaux Remèdes, June 24, 1912).

All that we have said in the preceding section in reference to **cool baths, dietary**, and general hygiene is equally applicable to this class of cases.

The writer advocates the use of alkalized **kefir**. To  $\frac{1}{2}$  a liter (1 pint) of kefir he adds  $\frac{1}{2}$  a liter (1 pint) water and 5 c.c. (80 minims) of a 20 per cent. solution of **sodium carbonate**. J. Peiser (*Monats. f. Kinderheilkunde*, Bd. xi, Nu. 5, 1912).

In the dysenteric form, **polyvalent anti-dysenteric serum** (both the Shiga and Flexner types) should be given at once. When the type of organism present has been determined, the indicated monovalent serum should be substituted. In the chronic stage preceding recovery, a diet rich in carbohydrates, such as **malted milk** or **dextrimaltose**, should be prescribed. Spence (*So. Med. Jour.*, Mar., 1922).

### CHRONIC DIARRHEA.

**Etiology.**—The chronic form of diarrhea is met with as the result of a previous acute attack or arises in an insidious manner from prolonged irritation of the intestinal canal by ill-digested and more or less fermenting food.

In those cases in which it is the result of an acute attack we have, as a rule, to deal with definite organic lesions. In some the persistent irritation is due to an ulceration of the intestinal wall, generally follicular, but occasionally catarrhal in character. In others we meet with an atrophic condition of the tubular glands and villi in the small intestines, associated with marked cell proliferations in the adenoid tissue of the mucosa (Holt). In a few instances the constitution of the infant has been so profoundly impaired by the acute attack that the various systemic functions are re-established with difficulty. Digestion continues to be imperfectly performed, and fermentation with the development of irritating and toxic products takes place, leading to a continued systemic

intoxication, which manifests itself in anemia, defective general nutrition, and an irritable nervous system, and is associated with persistent looseness of the bowels.

**Symptoms.**—Cases of chronic diarrhea form a considerable proportion of the diarrheas met with during the autumn. In the first class of cases the symptoms of acute inflammation have, to a great extent, subsided; the temperature remains, for the greater portion of the day, normal, and sometimes falls even below the normal line; pain and tenderness have almost entirely passed away, but the motions still remain too frequent; their odor is offensive, blood is occasionally seen in the form of minute dark specks, and mucus of a greenish or brownish color is still present in considerable amount. The consistence and color of the stools are variable. At one time they are of nearly normal consistence and fairly homogeneous; at other times they are quite fluid and associated with much flatulence. Prolapse of the bowel occurs only occasionally.

The appetite is very variable; vomiting may occasionally occur; but a fair amount of nourishment is generally taken during the twenty-four hours. Nevertheless, the infant remains pale and weak, and lies in a helpless and apathetic manner. As the disease progresses nutrition steadily fails, and weight is lost, chiefly through wasting of the subcutaneous tissues, so that the inelastic skin hangs in folds over the shrunken limbs. In many cases the abdomen may be distended, but in others it is soft and retracted. Palpation generally reveals the liver and spleen to be of normal size. The mesenteric glands through the abdominal walls can rarely be felt, although in post-mortem exam-

inations they are generally found to be enlarged. Petechial spots occasionally are seen on the abdomen and on the extremities. The circulation is very feeble. The lower limbs are always cold, sometimes cyanotic, and occasionally edematous. The urine is scanty. The nervous system suffers with the general failure in nutrition. The infant is peevish, easily disturbed, and sleeps badly at night.

The progress of these cases is by no means uniform. Some weeks may show a slight gain; but trivial causes, a chill to the surface of the body or a slight irregularity in feeding, may bring on a relapse, in which the gain is usually soon lost.

Complications are apt to arise. Thrush is not uncommon. The frequency of a latent otitis must always be remembered. Bronchitis is liable to appear and may develop into a pneumonia. Occasionally we meet with a general adenitis or a still more distressing furunculosis. Only rarely is nephritis encountered.

While a fatal termination occurs in a large percentage of these cases, in a few under careful dietetic and hygienic treatment the appetite gradually returns, the stools become more normal, nutrition gradually improves, and in time convalescence is thoroughly established.

In a second class of cases chronic diarrhea establishes itself without any preceding acute attack. Eustace Smith considers that in a considerable number the affection is due to repeated chillings of the surface of the body, producing a catarrhal condition of the gastrointestinal tract.

A faulty dietary is at all times an important factor, especially when associated with the depressing influence of unhygienic surroundings. This form

of diarrhea is frequently met with in foundling institutions and hospitals.

The onset of the attack is gradual and insidious. A failure to gain in weight or an actual loss may be the first symptom demanding attention. The evacuations will be found to be more frequent than normal, unduly large in amount, pale in color, and pasty in consistence. As the disease progresses the stools become quite frequent, at times frothy and sour-smelling, at other times thin, dark-colored, and offensive. The abdomen is distended. A cool perspiration occurs when the infant falls asleep. The urine becomes scanty and contains both indican and urobilin. The skin assumes an earthy hue, and the face acquires a curious look of old age. The infant lies in its cot in a helpless apathetic state, and makes its wants known by a scarcely audible whine. Such infants readily succumb to some intercurrent disease. Any of the complications which we have already referred to in connection with the preceding group may be met with in this condition. The mortality is very great.

**Diagnosis.**—It is often difficult in these cases to decide whether the condition present in the intestine is a sufficient explanation in itself of the serious failure in general nutrition, or whether we have, in addition, to deal with some underlying constitutional disease. The question will always be a difficult one, but the physician will act wisely if he bases his opinion upon the history of the case and the general condition of the patient rather than upon any one particular symptom or physical sign.

**Prognosis.**—The prognosis in cases of chronic diarrhea must always be very guarded. To some extent it is dependent upon the previous constitu-

tion of the infant, on the hygienic conditions obtainable, and upon the zeal and regularity with which all instructions are carried out. When ulceration is present to any considerable degree, the prognosis is always bad, although, under favorable conditions, not hopeless. In determining its existence our chief dependence must be placed on the previous history. The longer the inflammation has lasted and the higher has been the temperature, the greater the probability of ulcerative lesions (Holt).

**Treatment.**—With the conditions present in chronic diarrhea no good, but often harm, may result from the employment of ordinary astringent, or even antiseptic, remedies administered by the mouth. If drugs are to be given only those should be employed which will not disturb the stomach, and may, to some extent, improve general nutrition. Some cases among older infants do, undoubtedly, derive benefit from the prolonged administration of **iron**. It may be given in one of its acid preparations or in a neutral and less irritating salt. Nutrition may, to a small extent, be assisted by the inunction over the abdomen, or body generally, of codliver oil or cocoa butter. The moderate employment of stimulants is called for in almost all cases. Great attention must be given to the proper regulation of the **dietary**; to this end the stools should be frequently examined. Fats should be eliminated completely until distinct improvement sets in, and then only permitted in small amounts. Milk must be fat free.

**Buttermilk**, as recommended in the acute form of diarrhea, has, in my hands, often proved of value. Starchy foods should be more or less predigested.

Considerable benefit may be derived from the employment of scraped meat, meat juice, broths, and peptonized meat foods. No absolute rules can be laid down suitable for all cases, but each case must be studied by itself.

We have before insisted upon the necessity of placing the patient under the most perfect hygienic conditions attainable, and especially of securing an abundance of **fresh air**. In the treatment of those cases which are deemed to be dependent upon ulcerative conditions our chief therapeutic reliance must be placed on the careful use of astringent injections into the colon. Weak solutions of **silver nitrate** (1:2000 to 1:1000), or one of the **salts of zinc** (1:500 to 1:250), or of **tannic acid** (1:100), or of the fluidextract of **hamamelis** (5iv to Oj—16 to 30 c.c.), or the colorless fluidextract of **hydrastis** (5ij to Oj—8 to 30 c.c.) may prove of value. These injections should only be used after thorough irrigation of the bowel by **normal saline solution**, and to be of service should reach at least all the descending colon. This method of treatment may easily be overdone. Their too frequent employment has often appeared to depress the infant and to irritate the intestinal mucosa. Warm **injections of thin starch water** or of **gelatin** have, on the contrary, often a very soothing effect.

**Opium** should be made use of only to moderate excessive peristalsis, and in these cases it is best given in a little **starch water** by **rectal injection**. (For CHOLERA INFANTUM see Vol. III.)

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**DIATHERMY.** See ELECTROTHERAPEUTICS.

**DIAZO-REACTION.**—Ehrlich discovered that in certain pathological conditions the urine gave a deep-red color when treated with diazo-compounds and ammonia. This has been called the diazo-reaction, which normal urine never gives.

Von Jaksch (Clinical Diagnosis, 1897, p. 375) believes the reaction to be due to acetone. "Spath claims that the reaction should be ascribed to oxyproteic (uroproteic) acid, a recently discovered normal urinary constituent, in case the urine contained an increased quantity of this substance." (Diagnostic Methods, Sahli, 1909). Sahli attributes the reaction to a pathological decomposition of the proteids. Todd (Clinical Diagnosis, 1912) attributes the presence of acetone bodies in the urine to "some obscure metabolic disturbance resulting from digestion of fats." Clinical evidence does not show the reaction to be due to acetone or uroproteic acid, but shows rather that the reaction is due to an allied substance resulting from diseased metabolism, or, which is less probable, an overproduction of the named constituents occurring in sufficient quantities to give the test only in diseased conditions. C. S. Vivian (Med. Rev. of Reviews, Dec., 1912).

Two solutions are necessary:—

Solution "A" consists of  
*Sulphanilic acid* . . . 5 Gm. (1¼ drams).  
*Concentrated hydrochloric acid* ... 50 c.c. (1½ ounces).  
*Water* ..... 1000 c.c. (1 quart).

Solution "B" consists of a ½ per cent. aqueous solution of sodium nitrite.

**TEST.**—Fifty parts of solution "A" and 1 part of solution "B" are thoroughly mixed in a clean test-tube. To this is added an equal volume of urine, and the mixture is well shaken. A few drops of strong ammonia are allowed to run down the side of the test-tube. If the reaction is positive a red ring will be produced at the line of contact of the first mixture and the ammonia. Upon shaking, the

whole solution assumes a bright-red color, the same color being imparted to the foam. If allowed to stand about twenty-four hours a green precipitate forms at the bottom of the tube. Ehrlich regarded this as an especial characteristic of the true diazo-reaction, although it is not always present.

Normal urine gives an orange color when treated with the above solutions. Sometimes the urine assumes a yellow color before the addition of the ammonia, upon the addition of which it becomes a lighter yellow. This Ehrlich called the "egg-yellow reaction," and is supposed to be due to the presence of urobilinogen. This reaction is supposed to be especially indicative of the approaching crisis in pneumonia. If there is an excess of biliary pigment in the urine a dark discoloration may occur which becomes, upon boiling, a reddish-violet color.

New method of performing the diazo-reaction of Ehrlich. The writer employs paranitrodiazobenzol sulphate, known in commercial chemistry as azophorrot P. N. The test is performed in the following manner: A few granules of azophorrot P. N. are placed in a test-tube with water (tap water may be used). The tube is inverted once or twice. Enough of the reagent is thus dissolved in the cold for use in the test. The urine is treated carefully with potassium or sodium hydrate (not with ammonia) until a slight turbidity remains. The aqueous solution of azophorrot P. N. is then added. If a bright-red color appears and, after shaking, the foam is red, the reaction is positive. With an intense reaction the color is cherry red. In a large series of cases tested with this method and the original technique of Ehrlich, the results corresponded invariably. K. Feri (Wiener klin. Woch., Bd. xxv, S. 919, 1912).

Certain drugs, chrysarobin, opium, and the phenol derivatives, cause the urine to give an apparently positive diazo-reaction, which is not the true reaction. According to Wood the foam is more of a yellow color than in the true diazo; the green

precipitate never forms upon standing; the color is more permanent in the diazo, and does not fade upon the addition of a strong mineral acid. Burghart observed that a negative diazo-reaction occurred after such drugs as tannic acid, tannigen, and tannalbin had been given.

**SIGNIFICANCE OF THE DIAZO-REACTION.**—A positive diazo-reaction usually occurs about the fourth day in **typhoid fever**, and it was formerly supposed to be pathognomonic of that disease. Although usually present in typhoid fever, its presence alone does not warrant a positive diagnosis of this disease, while its absence does not indicate a negative diagnosis.

**Typhoid** bacilli can be found in the blood early in the disease, but less frequently thereafter, contrary to the experiences with the agglutination reaction which increases as the disease progresses. In the 167 cases reviewed, the diazo-reaction was positive in 65.2 per cent.; in 113 cases the leucocytes numbered less than 6000 in 63.6 per cent., up to 10,000 in 32 per cent. and over 10,000 in only 4.4 per cent., including 2 convalescents and an infant. The writer's experience thus emphasizes the diagnostic importance of the diazo-reaction and of hypoleucocytosis. Bacteriologic examination of the blood with Kayser's bile-tubes permitted an early diagnosis in 100 per cent. of the 16 cases examined during the first week. He regards paratyphoid as an entirely different disease from typhoid, his experience confirming the fact that infection is derived from meat, especially pork, or external contamination of foodstuffs, while typhoid is derived from human sources. Minertz (Med. Klinik, Sept. 25, 1910).

When in **typhoid fever** a urine shows the diazo-reaction, it becomes necessary, in order to avoid mistakes, to ascertain whether the reaction is not due to phenolphthalein. As the presence of this drug can be easily demonstrated by addition of alkalis it is only necessary to test the urine with a few drops of some alkali; a pink or reddish color shows the

presence of phenolphthalein. If this reaction is negative we have a true diazo-reaction. But in case this reaction is positive (the urine becomes red after the addition of alkalis), we may have the phenolphthalein reaction alone, or a true diazo-reaction, together with the reaction produced by phenolphthalein. In order to test the urine in such a case of a suspected "mixed" reaction, add a few drops of some acid to the test-tube in which there is a positive diazo-reaction. If the color disappears altogether and appears again only after the addition of enough alkali to render the mixture alkaline, the reaction is due to phenolphthalein alone. If after the addition of acid the color becomes lighter, but does not disappear completely and becomes more intense by addition of enough alkali to render the mixture alkaline, the reaction is due to the substance or substances producing the true diazo-reaction and also to the presence of phenolphthalein. Levison (Med. Rec., April 1, 1911).

A positive diazo also occurs in **measles, pneumonia, miliary tuberculosis, scarlet fever, diphtheria, erysipelas**, and rarely in **rheumatism** and **meningitis**.

Study of the diazo-reaction in **scarlet fever, diphtheria, and serum sickness** to determine its diagnostic value in cases of serum sickness exhibiting a scarlatiniform eruption. A large number of diphtheria cases develop serum sickness with rashes of a scarlatiniform, morbilliform, or urticarial nature. The first type offers the greatest diagnostic difficulty, as it develops from the second to the sixth day after administration of antitoxin. Kerr and Rivier found the diazo-reaction invariably absent in scarlatiniform erythema due to serum disease, and the latter found it positive in 56 per cent. of cases of scarlet fever. The writers studied altogether 502 cases as follows: 375 cases of scarlet fever, 56 cases of diphtheria, and 37 cases of serum sickness. The scarlet-fever cases showed the diazo-

## COMPARATIVE DIAGNOSIS OF TYPHOID BY THE WIDAL, DIAZO, AND RUSSO TESTS.

	WIDAL.	DIAZO.	RUSSO.
Appears when?	Appears in typhoid fever. Usually after first week.	Appears early in typhoid fever.	Appears in typhoid fever.
Relapses and complications.	Relapses or complications appear to have no effect on reaction.	Reappears with relapses but not with complications.	A positive reaction which grows in intensity probably points to a grave or fatal issue.
Reaction time?	Observations of 2 to 24 hours necessary.	Technic rapidly completed.	Technic rapidly completed.
Acute miliary tuberculosis.	Never present in this disease.	May appear in this disease.	Perhaps never present.
Always present in typhoid?	No.	No.	Yes, perhaps in every case of true typhoid.
In measles?	No.	Sometimes.	No.
In pneumonia?	No.	Sometimes.	?
In malaria?	No.	Sometimes.	No.
In small-pox?	No.	No.	Yes.
Chronic tuberculosis?	No.	Yes. Often occurs late in fatal cases.	Yes.
Effect of drugs taken internally?	None.	It is probable that no drug taken internally gives the true diazo reaction. Certain drugs may interfere with the positive test.	The positive test seems to be given by several drugs, notably urotropin.
Reaction late in typhoid?	The rule.	A diazo test which makes its first appearance after the second week points to acute miliary tuberculosis. When a positive reaction suddenly appears during convalescence a relapse is to be expected.	
Persistent reaction in typhoid?	Gives no diagnostic nor prognostic information.	May persist throughout infection without any special significance.	Persistent reaction probably spells a bad prognosis.

William (Archives of Diagnosis, Jan., 1912).

reaction positive in 8.53 per cent. The largest number of positive reactions occurred during the first week of the disease, when the rash was present, and gradually diminished and disappeared with convalescence. Uncomplicated cases of diphtheria showed a general average of 5.4 per

cent. positive. Rashes in serum sickness gave a general average of 10.8 per cent. positive. Sixteen cases of the scarlatiniform type showed 1 positive diazo, or 6.2 per cent. Of 18 urticarial types 2 were positive, or 11.1 per cent. In 3 cases of the morbilliform type none were positive.

In the 1 positive case of the scarlatiniform type, in which there were no other symptoms of scarlet fever, there ensued an uneventful recovery and no desquamation. The positive diazo here may have been due to the diphtheria. The writers place little value on the diazo-reaction as a point of differential diagnosis, because it is positive in only 15 per cent. of scarlet-fever cases during the first week, and because it was positive in 12.9 per cent. of diphtheria cases during the first week. The reaction was found positive in 75 per cent. of cases of measles. Therefore, a negative reaction in a case of morbilliform eruption would be of value in differential diagnosis between **serum sickness** and **measles**. S. S. Woody and John Kolmer (Archives of Pediatrics, vol. xxix, No. 12, 1912). H.

**DIETHYLBARBITURIC ACID.** See VERONAL.

**DIETHYLENEDIAMINE.** See PIPERAZIN.

**DIETHYLMALONYLUREA.** See VERONAL.

**DIGITALIS.**—Digitalis is officially defined as the dried leaf of *Digitalis purpurea* (Scrophulariaceæ). The plant is considered indigenous to central and southern Europe, and is found, among other localities, in the United Kingdom and especially Germany. It grows wild on gravelly or sandy soils in young plantations, at hedge-sides, and in hill-pastures, but is also extensively cultivated. It has been introduced in America, but is still grown more as an ornament to gardens and in hot-houses than for commercial purposes. Digitalis of excellent quality grows abundantly on the northern Pacific coast of the United States.

The digitalis plant, which is the source of all our medicinal preparations, is a biennial herb with an erect

stem twelve to fifty inches in height; numerous drooping, tubular, purple-spotted (occasionally white) or purple flowers, and large, alternate, ovate or ovate-lanceolate, crenate, rugose leaves. The latter are downy, especially on their grayish-green or -brown under surfaces; usually exhibit a purplish midrib, and taper into winged petioles.

The leaves constituting the official digitalis were formerly required to be of the second year's growth, but according to experts in these matters, fully developed leaves of the first year plant, collected toward the end of the season, are quite as active as those of the second year. Neither does the locality of growth necessarily exert as great an influence upon the activity of digitalis as has been asserted (Hale), although digitalis growing wild, especially in hilly districts (Butler), is generally believed to be more active than that which is cultivated. Although leaves grown in England have long been considered the best, Hale has demonstrated American leaves to be of equal value.

More important than the factors already referred to are the methods adopted in drying the leaves and storing the galenical preparations. The leaves should be dried in the dark, at a temperature not greatly exceeding 100° C. Properly cured, they exhibit a dark-green hue and an almost total lack of odor, except that generally possessed by dried herbs and leaves, which is frequently described as "tea-like." Once dried, the leaves should be kept in well-filled, dry, opaque and air-tight containers. In the German Pharmacopeia it is specified that both leaves and powder are to be kept over freshly calcined



lime, which absorbs any moisture present, and are to be discarded after a period of one year.

However carefully the drug may have been dried and stored, a more or less considerable deterioration, the rate of which cannot be definitely foretold, is likely to take place. This is true likewise of the fluid preparations of digitalis. Furthermore, as obtained by the physician, the fluid galenicals may not only be deficient in strength, but instead may err on the side of excessive potency, largely owing to the evaporation of the menstruum from imperfectly closed containers. Thus, Pittenger, testing 51 samples of digitalis tincture, observed a variation in their activity ranging from 30 to 444 per cent. (100 per cent. being standard strength), while 16 samples of digitalis fluidextract assayed at from 26 to 160 per cent. Goodall, testing 23 samples of the tincture freshly made by chemists of repute, found only 12 to be of average strength. In view of these pronounced discrepancies, and the possibility of consequent harm, exact clinical use requires that the digitalis employed shall have been physiologically standardized, either by the frog-heart permanent systole method or by the minimal lethal dose method in mammals, and that, in the case of fluid preparations, the containers in which the drug has been stored away shall have been kept tightly corked.

The U. S. Pharmacopœia, in recognition of the importance of proper standardization, especially since it has become customary to give digitalis in the maximum tolerated dosage, makes the following provision in this connection: "Digitalis, in the

form of the tincture, properly injected into the ventral lymph sac of a frog, has a minimum systolic dose (the minimum dose producing in one hour a stoppage of the ventricle of the heart in systole) not exceeding 0.006 c.c. of tincture, equivalent to 0.00,000,05 Gm. of ouabain, for each gram of body weight of frog."

That the standardization shall have been fairly recent is another important point, since leaves or galenicals assayed a year before may have lost a portion of their strength during that time.

The further danger which formerly sometimes arose from the substitution by unscrupulous druggists, in bottles bearing the labels of reliable pharmaceutical houses, of inferior preparations for the original properly standardized contents, has been lessened by the official adoption of the requirement of biological standardization.

Eight samples of digitalis fluidextract, made with 62.5 per cent. alcohol, showed an average annual loss in activity of about 4 per cent. Eleven samples of the fluidextract made with 48 per cent. alcohol showed an average loss of 10 per cent. per year. Six samples of digitalis tincture showed an annual loss of 9 per cent. Houghton and Hamilton (*Amer. Jour. of Pharm.*, Oct., 1909).

Among 23 samples of tincture of digitalis examined the limits of the variation were from 275 per cent. over strength to 40 per cent. under. It seems safe to believe that the tincture retains its full activity for one year, but that after that period deterioration of the drug is likely to have taken place. Goodall (*Brit. Med. Jour.*, April 20, 1912).

Digitalis deteriorates in the presence of water. It is irrational to dispense the tincture of digitalis already diluted with water, or with an

aqueous vehicle. The physician should order the necessary dilution to be made by the patient each time he takes the prescribed dose, or should employ a vehicle containing a sufficient amount of alcohol. R. A. Hatcher and Cary Eggleston (Amer. Jour. of Pharm., May, 1913).

Series of experiments carried out 1, to show that tinctures of digitalis deteriorate quite rapidly, and 2, to disprove the statements made at several medical society meetings, that fat-free preparations deteriorate more rapidly than the regular U. S. P. tincture. The physiologic assays were made on each of 15 samples 5 and 8 months, respectively, after the first test. Pittenger and Mulford, Jr. (Jour. Amer. Pharm. Assoc., Mar., 1918).

Series of tests showing that the rate of deterioration of tincture of digitalis varies greatly with different lots. While the great majority of samples deteriorate, and some deteriorate very rapidly, there are quite a few samples which apparently do not show deterioration at all, and in many cases preparations deteriorate rather rapidly during the first 3 months and then remain practically permanent. The average deterioration in 9 to 13 months of 43 samples was 18.8 per cent. The average deterioration of 38 samples during the first 3 or 4 months was 4 per cent. per month; of 32 samples after the first 3 or 4 months, 2.4 per cent. per month. P. S. Pittenger (Jour. Amer. Pharm. Assoc., Dec., 1918).

**CONSTITUENTS OF DIGITALIS.**—The active constituents of digitalis belong to the group of the glucosids,—relatively unstable substances as a rule, from which sugar is set free by certain enzymes or by heating with a dilute acid or alkali. The chief principles were isolated by Schmiedeberg and Kiliani:—

*Digitoxin*, a crystalline glucosid with well-defined chemical character-

istics, insoluble in water, very slightly soluble in ether, freely soluble in alcohol and in chloroform. This is the most powerful acting constituent of digitalis, and is contained in it to the extent of 0.2 to 0.6 per cent.

*Digitalin* (digitalinum verum), an amorphous glucosid considered chemically definite by Kiliani, and stated by him to be soluble in 1000 parts of water. It dissolves readily in alcohol, but slightly in chloroform and in ether.

*Digitalein*, an amorphous, glucosidal body, considered a definite compound by Kiliani, but accepted by Kraft only as a generic term for all the active digitalis glucosids that are soluble in water. Thus, there may exist several digitaleins, all having this property.

*Digitophyllin*, a crystalline glucosid isolated by Kiliani from the leaves of digitalis, and not present in the seeds. It is soluble in alcohol, but almost insoluble in water. By some it is considered identical with the substance widely used in France, known as "digitaline cristallisée."

All the above are therapeutically active. The following is of little or no value in this respect:—

*Digitonin*, a substance belonging to the group of saponins. Amorphous digitonin is soluble, but the crystalline almost insoluble in water. The substance is also fairly soluble in alcohol, but practically insoluble in ether and chloroform. According to Kiliani digitonin is present only in the seeds of digitalis. Kraft, however, refers to a similar body which is contained in the leaves. Digitonin possesses the useful property of keeping the insoluble glucosid digitoxin in solution in aqueous preparations of digitalis, such as the infusion, or when the digitalis leaf is taken by the mouth.

Other substances contained in digitalis include *digitin*, an inert crystalline substance; *gitalin*, a physiologically active glucosid; *digitalosmin*, a stearoptene imparting to digitalis its odor and an acrid taste; *digitoflavone*, a yellow pigment; also a red pigment; an oxidizing ferment occurring in leaves recently dried, and ash to the extent of 10 to 16 per cent.

Most preparations of the separated active principles of digitalis on the market are obtained from the seeds.

#### PREPARATIONS AND DOSE.

—The following preparations of this drug are recognized:—

*Digitalis*, U. S. P., the dried leaf. Dose,  $\frac{1}{2}$  to 3 grains (0.03 to 0.2 Gm.); average  $1\frac{1}{2}$  grains (0.1 Gm.).

*Infusum digitalis*, U. S. P. (infusion of digitalis), prepared by adding to 15 Gm. of digitalis in fine powder 700 c.c. of boiling water, covering tightly, allowing to macerate for one hour, filtering, adding 100 c.c. of alcohol and 150 c.c. of cinnamon water to the filtrate, passing enough cold water through the residue on the filter to make 1000 c.c., and mixing well. Dose, 1 to 4 fluidrams (4 to 16 c.c.); average,  $1\frac{1}{2}$  fluidrams (6 c.c.).

*Tinctura digitalis*, U. S. P. (tincture of digitalis), 10 per cent., prepared by percolation and maceration. Biologically assayed: "Tincture of digitalis, injected into the ventral lymph sac of a frog, has a minimum systolic dose of not less than 0.0055 c.c. and not more than 0.0065 c.c., equivalent to not less than 0.00,000,046 Gm. and not more than 0.00,000,054 Gm. of ouabain, for each Gm. of body weight of frog." Dose, 5 to 30 minims (0.3 to 2 c.c.); average, 15 minims (1 c.c.).

*Fluidextractum digitalis*, N. F. (fluid-extract of digitalis), prepared by per-

colation of the powdered leaves with diluted alcohol. Biologically assayed. Dose,  $1\frac{1}{2}$  minims (0.1 c.c.).

The following preparation is no longer recognized:—

*Extractum digitalis*, U. S. P. VIII (extract of digitalis), prepared by evaporating the fluidextract until it is reduced to a pilular consistence. Dose,  $\frac{1}{5}$  grain (0.012 Gm.).

The active substances present in the infusion of digitalis appear to be almost exactly the same as in the tincture. It is stated, however, that a greater relative proportion of digitoxin is present in the latter and larger amounts of digitalein and digitonin in the former.

Though in most cases the tincture suffices, sometimes other preparations are better tolerated. In not a few the powdered leaf or some of the similar preparations are borne in sufficient unit-dosage when the patient is intolerant to satisfactory doses of the tincture. The leaves, prescribed with sodium bicarbonate combined with quinine or given with various digestives, may occasionally be also very effectively employed instead of the tincture. Harlow Brooks (Trans. Coll. Phys. of Phila., 1925).

The following unofficial preparations of or derived from digitalis have come into use:—

*Digitalin*, German (*digitalinum germanicum*), a mixture of glucosids obtained from digitalis seeds by extraction with alcohol, precipitation with tannic acid, decomposition of the tannate with acetate of lead or zinc, and purification of the residue. The glucosids present are said to include about 50 or 60 per cent. of digitonin, one-tenth that percentage of true digitalin, as well as digitalein. The substance occurs as a yellowish, amorphous powder, and has the valu-

able property of being entirely soluble in water as well as in alcohol, though it is insoluble in ether and chloroform. It can be given hypodermically, and is claimed not to produce gastric irritation when taken by mouth, except in large doses. The ordinary dosage varies from  $\frac{1}{12}$  to  $\frac{1}{3}$  grain (0.005 to 0.02 Gm.); in emergencies, doses of  $\frac{1}{2}$ , 1, or even 3 grains (0.03 to 0.2 Gm.) may be given.

The official tincture of digitalis is absorbed more rapidly from the gastrointestinal tract of cats than is the infusion. Digalen is likewise absorbed more rapidly. Haskell, McCants and Gardner (*Arch. of Internal Med.*, Aug., 1916).

The infusion should be discarded in 3 to 5 days, unless kept at low temperature, when the time may be extended to 6 to 7 days. Pomeroy and Weyl (*Amer. Jour. of Pharm.*, xcii, 394, 1920).

Testing 15 samples of the infusion from retail pharmacies by the Hatcher and Brody cat method, the writer found that the 5 prepared by simple dilution of the fluidextract averaged 62.6 per cent. of theoretic activity, while the 10 prepared by the U. S. P. method averaged only 38.1 per cent. He stresses the need of an improved method of preparing the infusion. A. R. Bliss, Jr. (*Jour. of Lab. and Clin. Med.*, Jan., 1922).

Digitoxin (digitoxinum), a single glucosid obtained from digitalis leaves by extraction with 50 per cent. alcohol, precipitation of useless material with lead acetate, evaporation of the supernatant fluid, repeated extraction of the residue with ether, and crystallization. Two forms, hydrated and anhydrous, respectively, are obtained, according as the digitoxin is crystallized from alcohol or from a chloroform-alcohol mixture. The anhydrous form is official in the French Pharmacopeia (Codex) as "digitaline

cristallisée" ("digitoxine"; "digitaline Nativelle"), and is extensively used in that country. Digitoxin is insoluble in water, but dissolves in 43 parts of 90 per cent. alcohol and is easily soluble in chloroform. If given subcutaneously, digitoxin sometimes produces marked local irritation. The single dose of digitoxin is usually stated as  $\frac{1}{250}$  grain (0.00025 Gm.), but amounts as large as  $\frac{1}{64}$  grain (0.001 Gm.) and even  $\frac{1}{20}$  grain (0.003 Gm.) (Corin) have been given. The maximum daily dose is  $\frac{1}{64}$  to  $\frac{1}{20}$  grain (0.001 to 0.003 Gm.). "Digitaline chloroformique" ("digitaline amorphe"; "digitalinum gallicum"; Homolle's digitalin) is a body probably consisting chiefly of digitoxin, and which is completely soluble in chloroform. It was formerly the official French "digitaline," but is now replaced by "digitaline cristallisée." The dose is generally stated to be the same as that of the latter.

Use of French crystallized digitalin recommended. There are three ways in which it may be prescribed. First, in massive doses. Fifty drops of the 1 in 1000 solution should be given once or twice in one day in those cases where asystole is threatening, and where there are edema, visceral congestion, deficient urinary elimination, etc. After thirty-six to forty-eight hours abundant diuresis sets in, and the cardiac contractions increase in strength. Secondly, in small doses. These are indicated in cases of palpitation, cardiac erethism, and for the dyspnea of mitral stenosis (during compensation). From 5 to 10 drops of the same strength of solution should be given daily for five consecutive days, and then omitted for three or four weeks, when these doses may be recommenced. Thirdly, in very small doses as a cardiac tonic. From 2 to 4 drops of the solution may be

given daily for weeks or months, omitting the doses every two or three weeks for one or two weeks. When a rapid action is required, crystallized digitalin dissolved in oil may be injected under the skin, without any subcutaneous irritation; from  $\frac{1}{8}$  to  $\frac{1}{2}$  mg. ( $\frac{1}{500}$  to  $\frac{1}{30}$  grain) may be so injected. Huchard (Jour. des Prat., Dec. 1, 1906).

Digitalinum verum (Schmiedeberg's digitalin), considered a definite chemical compound, has been used with asserted good results, more especially in the milder forms of cardiac insufficiency, by some clinicians. It is best given in dilute alcohol, in which it readily dissolves, but has also been administered in pills. Kobert states the maximum single dose to be  $\frac{1}{16}$  grain (0.004 Gm.) and the daily dose  $\frac{1}{8}$  grain (0.008 Gm.), while Mottes recommends that  $\frac{1}{250}$  grain (0.00025 Gm.) be given every two or three hours. The average single full dose may be stated as  $\frac{1}{32}$  grain (0.002 Gm.).

Digitol, a "fat-free tincture," i.e., one from which the fixed and volatile oils which are supposed to contribute to the gastrointestinal irritation sometimes produced by digitalis have been removed. Dose, same as of the official tincture.

Digitalone, a sterile, non-alcoholic preparation of the same strength as the tincture, containing chloretone as a preservative, and suitable for hypodermic use. Dose, same as the preceding.

Digalen (liquor digitoxini solubilis), a solution said to contain 1 part of Cloetta's "amorphous soluble digitoxin" in 1000 parts of glycerin and 1600 parts of distilled water, with  $7\frac{1}{2}$  per cent. of alcohol added. The nature of Cloetta's principle, which is said to be about 5 times as soluble as

crystallized digitoxin and is prepared by a secret process, is not known. Kiliani believes it to be merely an amorphous substance containing a high percentage of digitalein. By some it is claimed to be the form in which digitoxin is present in the digitalis leaf. Digalen may be used by mouth or intravenously; according to Pagliano, intramuscular injections are well borne. Dose, 8 to 32 minims (0.5 to 2 c.c.); maximum daily dose, 96 minims (6 c.c.). Digalen tablets are also available.

Upon extracting the amorphous digitoxin, so called, from digalen tablets and using it in solution in saline, the drug was found to be equal in activity to crystalline digitoxin; the fatal dose per gram of frog was 0.0085 mg. Cary Eggleston (Amer. Jour. of Pharm., March, 1913).

Digipuratum, a greenish-yellow, bitter-tasting powder, obtained by removing about 85 per cent. of the inert and undesirable constituents from an alcoholic extract of digitalis by the addition of ether, petroleum benzin, or other precipitant, and reducing the resulting fluid to a powder by evaporation with milk-sugar. The preparation is biologically standardized and is said to contain 0.4 per cent. of digitoxin and 4 per cent. of digitalin in the form of tannates. Its active components are soluble in weak alkalis, but not in cold water. It is supplied in tablet or powder form, and the average dose is  $1\frac{1}{2}$  grains (0.1 Gm.).

Digipuratum is not entirely free from after-effects. The usual daily dose is 3 tablets, but with individuals over 40 years old, particularly with alcoholics, smokers or gouty patients, it is advisable to begin with half the dose, since the stomach frequently will not tolerate larger amounts. The same care is

necessary in pronounced arteriosclerosis or contracting kidney. Veiel (Munch. med. Woch., Sept. 27, 1910).

Digipuratum is insoluble in cold water and dilute acids, but it is soluble in 0.1 per cent. sodium bicarbonate. It has about half the toxicity of ordinary digitalis leaves (Schuttler). It keeps well, is uniform in composition, contains all the glucosides of value in digitalis, and causes less gastric irritation than the powdered leaves. Mueller states that its effect is apparent on patients after 0.4 Gm. (6¼ grains) on the second day, and after 0.3 Gm. (5 grains) on the third day. W. E. Dixon (Quarterly Jour. of Med., No. 18, 1912).

Digitalysatum, a fluid prepared by dialysis from the fresh undesiccated digitalis plant. Each gram (16 minims) is stated to represent 0.12 Gm. (2 grains) of powdered digitalis leaves. The product contains 12 per cent. of alcohol. It is employed in doses of 5 to 15 minims (0.3 to 1 c.c.), internally or subcutaneously.

**MODES OF ADMINISTRATION.—Oral.**—Digitalis is usually administered by mouth, either in the form of the tincture, the infusion, or the powdered leaves. The question as to which of these preparations is the best has given rise to much discussion. Most clinicians consider that where both cardiotonic and diuretic effects are desired the infusion is most efficient, while under all other conditions the tincture should be used. German clinicians, however, manifest a general preference for the powdered leaves, notwithstanding the fact that these are probably somewhat more irritating to the stomach than the other preparations and perhaps less certain in absorption.

The various unofficial preparations of the digitalis glucosids are not, on

the whole, considered in any way superior to the official galenicals, except in the fact that glucosids kept in the dry form are likely to preserve their efficiency for a longer time than the leaves, and are thus, where there is no certainty of securing fresh, undeteriorated galenicals, more reliable than the latter. Allbutt, for intermittent administration, speaks favorably of granules of the digitalins of Nativelle or Homolle.

Since the effects of digitalis administered by mouth take several hours to appear and, when once established, last for some days after a single dose, it is unnecessary to give the drug oftener than two or three times daily. It is usually administered with or just after meals, though Worth Hale, having found that the gastric juice tends to impair the activity of digitalis, recommends that the drug be taken between meals and a large quantity of water simultaneously ingested to diminish the resulting gastric irritation. According to Allbutt, combination of the drug with a cordial and light bitter, and requiring the patient to rest for half an hour after the digitalis has been taken, will tend to avoid the production of nausea. The infusion might also be iced, or given in an effervescent preparation. Digipuratum has been stated by several observers to be better borne by the stomach than the official preparations.

The dosage of digitalis is a matter usually requiring very careful consideration. The variations in the amount required in the treatment of different cardiac lesions will be referred to in the section on THERAPEUTICS, but certain general facts

may appropriately be referred to here. The chief criterion for judging of suitable dosage is in most instances the degree of relief experienced by the patient from the various symptoms of cardiac inefficiency. While in some cases the dose may have, sooner or later, to be increased to considerably beyond the average amount, the aggregate of the earlier doses, except in emergencies, should be relatively moderate, so that if toxic symptoms appear, destruction of the excess of drug present in the body can be soon effected. The pulse rate should be carefully watched, and the urinary output in particular be observed, any tendency to diminution of the latter—except immediately after the removal of edema with diuresis—leading to a suspicion that the dose given is too large and is inducing renal vasoconstriction. Riegel emphasized the fact that, in **chronic myocarditis** especially, excessive doses of digitalis might suddenly lead to suppression of urine. Likewise where, in conjunction with pronounced edema, renal activity is poor, toxic phenomena are apt to appear from large doses, and the amounts given should therefore at first be moderate.

In patients who have been taking digitalis for some time, intermission for an undue period is apt to result in a more or less serious setback in the general condition, even though, as is now believed, true habituation to digitalis, other than that implied in an increased ability of the gastrointestinal tract to eliminate the drug unabsorbed, is a practically negligible quantity.

In a review of newer concepts in digitalis therapy the writer gives the

following dosage for the oral use of the remedy:

*Small Dose Method.*—From 4 to 6 days are generally required for digitalization by this method; 2 to 4 grains (0.12 to 0.25 Gm.) of the powdered leaf or 20 to 40 minims (1.25 to 2.5 c.c.) of the tincture should be administered every 4 hours—4 doses daily—and continued until digitalization is induced. With weak or poorly absorbed specimens of digitalis full digitalization may not be secured at all by this method or it may require 10 days or more to secure it.

*Large Dose Method.*—From 1 to 2 days are required for digitalization. During the first 24 hours a dose of 6 grains (0.4 Gm.) of the powdered leaf or 1 dram (4 c.c.) of the tincture should be administered every 6 hours, day and night for 4 doses. On the second day the dose should be reduced one-half and the interval may be shortened to 4 hours, giving 4 doses per day and none at night. This latter dose and interval should be continued until full digitalization is secured.

*The Body Weight Method.*—This method permits full digitalization within 10 to 20 hours from the beginning of administration and is specially serviceable in cases manifesting urgent symptoms. Its use has proved so satisfactory during the 5 years since its introduction that it has been possible very largely to do away with the necessity for the intravenous or intramuscular administration of ouabain, strophanthin or other digitalis preparation. Cary Eggleston (Amer. Jour. Med. Sci., Nov., 1920).

Meyer warns against abandoning digitalis in cases where it does not seem effective at first. Thus, while in acute inflammatory states of the heart the drug is seldom of value, it may yield brilliant results later on. The same may be true in chronic disorders; in particular, where treatment with full doses may have proven a failure, smaller amounts may be found distinctly beneficial.

Eggleston's physiologic dose, if given in 18 hours, is not safe outside of a hospital. In severe cases, however, the writer has often given such a dose within 48 hours. J. G. Carr (Jour. Iowa State Med. Soc., Dec., 1921).

There is no real preference, for the average cardiac case, between the single massive dose, a modified massive dose method, or regularly repeated small doses. The chief difference is the time required to produce a result. In a few very severe cases the modified, massive dose method is preferable, and occasionally the single massive dose may be life-saving. The safe dose for continued use is 1 to 1.5 c.c. of the tincture a day. Christian (Boston Med. and Surg. Jour., July 13, 1922).

Of the drugs not infrequently given in combination with digitalis, nitrites require chief mention. The object in administering such vasodilators is to avoid any blood-pressure-raising effect of digitalis in patients already presenting high tension, especially where there is pronounced arteriosclerosis. Nitroglycerin, given at shorter intervals than the digitalis itself, is most frequently used. Where the blood-pressure, however, is not already high, and vascular changes are not marked, combination of nitrites with digitalis is without advantage and may actually hinder the good effects of the drug. Huchard advised the use of theobromine with digitalis where the pressor effect of the latter is feared, while Traube recommended that in cases of high blood-pressure laxatives be given as a preliminary measure.

Many writers advise the giving of vasodilators to counteract the constrictor effect of digitalis. It is high time that we discard this hoary tradition. Most of the work done on digitalis has been with toxic doses, and vasoconstriction is one of the toxic effects. It has been shown clinically that in the majority of patients with beginning

digitalis effect the blood-pressure falls. Conclusive proof that digitalis in clinical doses relaxes the peripheral vessels has been given by O. Müller and his pupils, who showed with the plethysmograph that there is a constant increase in the volume of blood in an extremity after the use of digitalis. Schmoll (Amer. Jour. Med. Sci., Jan., 1911).

For diuretic purposes such drugs as theobromine and theophyllin, squill, calomel, and the saline diuretics are frequently given with digitalis, the object being to supplement the cardiac and renal vasodilator diuretic effects of digitalis by direct stimulation of the kidney parenchyma or other contributory influences. Whitla considers agurin more effective than diuretin; he points out also that in rheumatic or gouty patients salicylates may be advantageously combined with digitalis for diuretic purposes.

The following pill is advised by Huchard and Fiessinger for combined cardiotonic, cathartic, and diuretic effects:—

℞ *Pulveris digitalis*,  
*Pulveris scilla*,  
*Pulveris scammonii*...ãã gr. xv (1 Gm.).

M. et ft. in pil. no. xx.

Sig.: Four to six pills daily.

It is often of decided advantage to combine digitalis with ergotin. In this way a pronounced diuretic effect may be obtained even when a combination of digitalis with the modern diuretics has failed. The author uses the following formula:—

℞ *Pulv. digitalis*.. 1.0 Gm. (15 grains).  
*Hydrargyri chloridi mitis* ... 2.0 Gm. (30 grains).  
*Scilla* ..... 3.0 Gm. (45 grains).  
*Ergotin* ..... 4.0 Gm. (60 grains).

M. et ft. in pil. no. xl.

Sig.: Four to six pills daily.

If the circulatory disturbance returns and the pills are again indicated, the following formula may be substituted:—



℞ *Pulv. digitalis* gr. xv to xxxviii (1.0 to 2.5 Gm.).

*Hydrargyri  
chloridi*

*mitis* ..... gr. viii (0.5 Gm.).

*Ergotin* ..... gr. xxxviii (2.5 Gm.).

*Scilla* ..... gr. xlv (3.0 Gm.).

M. et ft. in pil. no. 1.

Sig.: Two pills three times daily. A. Hecht (Therap. d. Gegenwart, Mar., 1911).

*Atropine* or *belladonna* may be used with digitalis where undue vagus stimulation and excessive slowing of the heart are to be avoided, but are disadvantageous in that they reduce secretory activity, thereby impairing digestion, and tend to counteract the diuretic effect of digitalis.

The writer cites Deschamps' recent thesis which reported 6 failures and 1 success in 7 cases of **auricular fibrillation** treated with quinidine alone, and 10 successes with 8 failures in 18 cases in which the quinidine had been preceded by a course of digitalis regardless of whether or not the heart showed signs of insufficiency. Cheinisse (Presse méd., Aug. 26, 1922).

Quinine in small doses is not infrequently of value when combined with digitalis in **chronic myocardial disease**, while iron is indicated in the numerous cases of **valvular disease** in which there is anemia:—

℞ *Tinctura digitalis*,

*Tinctura ferri chloridi*,

of each ..... f3iij (12 c.c.).

*Acidi phosphorici diluti*. f3ij (8 c.c.).

*Aque chloroformi*, q.s.

ad ..... f3viii (240 c.c.).

M. Sig.: Two teaspoonfuls in a half-glassful of water four times daily. (Whitla.)

Rest in bed and, where edema is present, a reduction of the fluids ingested are valuable adjuncts to digitalis therapy. In severe cases Huchard gave 5 ounces (150 c.c.) of milk mixed with 1½ ounces (50 c.c.)

of water four times daily for three days, and thereafter undiluted milk, until the patient ceased losing weight from the digitalis diuresis, when solid food was resumed and the amount of fluids increased. Removal of salt from the diet is another procedure which in a certain proportion of cases materially favors the elimination of dropsical accumulations, and may thus assist the diuretic effect of digitalis.

In children digitalis can usually be given in doses slightly larger than would be indicated by Young's rule. Thus, to patients 6 to 10 years old, one-half the adult dose may be administered. For infants 6 months old ¼ to 1 minim (0.015 to 0.06 c.c.) of the tincture may be used (Griffith). As in adults, a close watch should be kept on the action of the drug, and the dosage modified as required by individual peculiarities or the strength of the preparation used. Allbutt referred to the following combination as suitable for children:—

℞ *Infusi digitalis*,

*Infusi sennæ*,

*Infusi calumbæ* ..... āā 3j (4 c.c.).

M. Sig.: Three times daily before meals.

**Hypodermic Administration.**—In whatever form used, digitalis is almost certain to cause more or less local irritation when given hypodermically, and this route is therefore, on the whole, useful only for emergency cases, or where with the patient in a serious condition the stomach rebels upon oral administration. Either the tincture or the fluidextract may be used, though both have the disadvantage of including alcohol, itself an irritant. Among the unofficial preparations most frequently employed are digitol (a "fat-free" tincture),

digalen tablets, digitalone (said to be least irritating when fresh), and German digitalin. Digitoxin may be injected in the following solution (Unverricht):—

R *Digitoxin* ..... gr.  $\frac{1}{6}$  (0.01 Gm.).  
*Alcoholis absoluti* ... m℥ (5 Gm.).  
*Aquæ destillatæ* ..... ℥ss (15 Gm.).

M. Sig.: Inject 8 to 16 minims (0.5 to 1 c.c.).

Strict aseptic precautions are to be taken in administering an injection of digitalis; abscess formation will then seldom occur. The injection should be given deeply. To reduce the local pain, cold compresses are of value.

**Rectal Administration.**—Where digitalis causes gastric disturbance and hypodermic administration is impracticable, the remedy may be given by rectum, though absorption by this route is somewhat uncertain. Krehl uses for this purpose an infusion of 30 grains (2 Gm.) of digitalis in 5 ounces (150 c.c.) of water, which is mixed with  $1\frac{2}{3}$  ounces (50 c.c.) of gum-arabic mucilage. The mixture thus obtained is intended for four enemas, two or three of which may be given in a day.

When frequent vomiting prevents absorption from the stomach, 2 other paths of absorption are available: the rectum and the subcutaneous tissues. Half an ounce (15 c.c.) of infusion, per rectum, 3 times a day, will give about as prompt results as the drug given by mouth. Janeway (Amer. Jour. Med. Sci., June, 1908).

Digitalis was used by the rectum 26 times in 19 patients with **auricular fibrillation**, employing a purified aqueous solution of digitalis leaves. One cubic centimeter contained the equivalent of 0.1 Gm. of powdered leaf. The amounts given ranged from 8 to 20 c.c. With one exception, the total dose was administered at one time. A desirable effect was apparent in every instance.

In many patients, the results were dramatically rapid and beneficial. Most of the digitalis given by rectum reaches the heart via the mesenteric and portal veins and not by way of the inferior vena cava. Rectal digitalis therapy is intended to supplement, not supplant, the oral method of administration. It is useful in the presence of nausea and vomiting, or after surgical operation, when oral medication is not feasible. The dose is comparable to that employed when a large single dose is given by mouth. Levy (Arch. of Intern. Med., June, 1924).

#### **Intravenous Administration.**—

Owing to the insolubility of the more active glucosids of digitalis, strophanthin, which is soluble in water, is better suited for intravenous use, and is generally employed instead. If it is desired to use digitoxin, chloroform or alcohol, or both, will have to be employed to keep it in solution, according to the variety of glucosid to be injected.

The intravenous or intramuscular use of digitalis is justified only when it is imperative that the effects be induced in 2 hours or less. In this event the writers advise strophanthin or crystallized ouabain. Great care must be taken if the patient has recently received digitalis. When nausea or vomiting, not due to digitalization, precludes oral use, the tincture may be given by rectum in like dosage until these symptoms cease. Children require somewhat larger doses per kilo. than adults. Robinson, White, Eggleston and Hatcher (Jour. Amer. Med. Assoc., Aug. 16, 1924).

**INCOMPATIBILITIES.**—Digitalis is incompatible in fluid preparations with salts of iron and lead, and with cinchona. It is likewise incompatible with tannic acid and all vegetable solutions containing it.

**CONTRAINDICATIONS.**—Absolute contraindications for digitalis are

few. The most positive are aortic aneurism in its later stages, partial heart block, cerebral hemorrhage, and recent embolism.

In the presence of pronounced arteriosclerosis caution in the dosage is necessary, and where the blood-pressure is very high it is probably best under most circumstances not to administer the drug. The capacity of digitalis directly to raise the blood-pressure by constricting the vessels, however, appears, on the whole, to have been unduly emphasized. Riesman points out the fact, moreover, that in cases of "high-pressure hypertrophy," *viz.*, where the blood-pressure is high and the heart enlarged owing to some obscure cause, but the arteries remain soft, dyspnea and vertigo are frequently relieved by small doses of digitalis, *e.g.*, 5 to 10 minims (0.3 to 0.6 c.c.) of the tincture or  $\frac{1}{4}$  to 1 grain (0.015 to 0.06 Gm.) of the powdered leaves, three times daily.

Digitalis is absolutely forbidden in cases of partial heart block. We should hesitate to use it in cases of recent emboli, cerebral hemorrhage, aortic aneurism and uremia, unless the need for it is imperative. In the tachycardia of hyperthyroidism and of cardiac neurosis it is useless and may do harm. Occasionally idiosyncrasy is encountered. A. E. Taussig (*Interstate Med. Jour.*, Aug., 1912).

A heart that is dilated or in danger of being dilated needs digitalis, but in sufficient doses to counteract the dilatation. The doses needed may be much more than those usually employed. O. H. Brown (*Jour. of Lab. and Clin. Med.*, May, 1923).

When given orally in large doses digitalis, in cases of myocardial insufficiency, improves all symptoms, promotes diuresis, reduces edema and decreases the size of the liver. This is not due to a change in the ventricular

rate but to increased muscular efficiency. It corresponds with the benefit obtained in auricular fibrillation. Luten (*Arch. of Intern. Med.*, Feb., 1924).

In cases with cardiac fibrosis (chronic myocarditis) and, especially, fatty degeneration digitalis is inefficient in proportion to the degree of morbid involvement, but is by no means absolutely contraindicated when signs of insufficient cardiac activity appear. The chief precaution to be exercised where these conditions are suspected is to use relatively small doses, in particular where the myocardial changes are considered to be very pronounced.

Dropsical patients who have taken large doses of digitalis for some time should be tapped with care, for the sudden withdrawal of the fluid may cause absorption of enough of the drug to poison the patient. Zemp (*Jour. Amer. Med. Assoc.*, xlix, 1349, 1907).

The irritant effect of digitalis in the stomach contraindicates its administration by mouth in the presence of gastric inflammation, unless there are urgent reasons for its use.

Not properly classified as contraindications, but none the less requiring emphatic mention, are certain conditions in which, though digitalis may or may not actually be indicated, according to circumstances, the physician is often tempted to administer the drug as a matter of routine, without stopping to inquire whether or not its use is warranted in the individual case. Among these are such vague conditions as "heart disease" in general, murmurs, palpitation and pain in the precordial region, none of which indicate digitalis except under certain definite conditions, to be set forth in the section of this article on THERAPEUTICS.

Caution is also required, in administering digitalis to a patient seen for the first time, to make sure that he has not just previously been taking the drug in large amounts, as it is by no means impossible to witness digitalis intoxication and even death (Eggleston) as the result of summation of the effects of large doses. This is all the more imperative since some of the forms of cardiac irregularity resulting from digitalis itself can easily be mistaken for those actually due to disease of the heart, and the new attendant will at once naturally think of subduing the disturbance, as, *e.g.*, in auricular fibrillation, with full doses of digitalis.

A patient taking digitalis should be carefully watched, especially the pulse. If the latter drops below 60 the drug should be suspended. It should also be discontinued when bigeminal heart action is present; this is most frequently observed with mitral lesions. Where, under digitalis, the amount of urine increases very rapidly, delirium may be observed, even although no digitalis is being taken at the time. This delirium might be ascribed to an autointoxication from absorption, as it coincides with the subsidence of the edema. Eichhorst (Deut. med. Woch., Jan. 2, 1905).

Case of a man who was admitted to a hospital in a condition of marked digitalis intoxication. For eighteen days he had been taking daily 4 powders each containing 0.1 Gm. ( $1\frac{1}{2}$  grains) of digitalis leaf and 0.5 Gm. ( $7\frac{1}{2}$  grains) of diuretin. Besides, while still at home, he had been given for three days, in addition to the powders, 2 granules of 0.0001 Gm. ( $\frac{1}{6750}$  grain) of "crystallized digitalin." The hospital interne, seeing a man markedly dyspneic and dropsical, prescribed further 50 drops of digitalin. The breathing was of Cheyne-Stokes type, the pulse-rate 36 to 38, and upon auscultation, in addition to the usual heart sounds, two

somewhat weaker sounds were heard at each cycle. That a typical coupled and even triple beat was present was illustrated by sphygmography. The blood-pressure (Pachon instrument) was 210 mm. Hg. The disturbance of rhythm persisted for over ten days, then gradually disappeared, while the pressure fell to 180 mm. Injection of 0.002 Gm. ( $\frac{1}{2}$  grain) of atropine during the period of coupled beats brought about no change. Roch (Revue méd. de la Suisse rom., Feb., 1913).

### PHYSIOLOGICAL ACTION.—

**Locally**, digitalis acts as an irritant. Thus, when applied to the mucous membranes it may cause redness and pain, and, if given subcutaneously, inflammation, leading occasionally to the formation of an abscess, even though no infective organisms have been introduced at the time of injection. The several glucosids appear to differ in their irritant properties, digitoxin being the most active, while digitalin is relatively but slightly irritating.

The digitalis bodies vary in their irritant action on a given mucous membrane. Moreover, one of these agents may be intensely irritant to one mucous membrane in a certain animal and yet without appreciable influence on the mucous membrane of another area. Hatcher and Eggleston (Jour. of Pharm. and Exp. Therap., Nov., 1912).

In the stomach, even moderate doses, especially when continued for some time, tend to induce a more or less marked irritation. The symptoms witnessed are not believed to be wholly due, however, to the local effect, as the drug is known to stimulate directly the vomiting center. This question will be considered further under UNTOWARD EFFECTS (*q.v.*).

**General Effects.**—*Nervous System.*—The nervous effects of digitalis are limited, probably even with the

largest poisonous doses, to the medulla and its contained centers. Moderate doses stimulate only the cardioinhibitory and vasoconstrictor centers. Larger doses, such as are frequently used in animal experimentation, excite, in addition, the vomiting and respiratory centers. Emesis occurs in those animals, such as the dog and cat, which are able to vomit, and in all, at a rather late stage in the poisoning, there is frequently noticed an acceleration in the breathing, the rate of which may be so increased as nearly to equal that of the heart. This respiratory change is probably not wholly due, however, to a direct effect of the drug on the center, but, at least in the more severe or actually fatal cases of poisoning, to the venous character of the blood, which very evidently plays an important part in bringing on the final lethal result; the respiratory acceleration—at first often with maintenance or an actual increase of depth—may thus in some cases be looked upon as an expression of physiological compensation rather than as the direct effect of the drug on the centers. The convulsions sometimes witnessed late in digitalis poisoning are believed due, at least in some instances, to medullary stimulation.

• In the frog the reflex excitability of the spinal cord is often diminished by digitalis.

*Circulation.*—The circulatory effects of digitalis are of paramount importance. In therapeutic doses the drug acts, in the first place, as a powerful stimulant to the myocardium itself. It increases the irritability, tonicity, and contractile power of the heart, although the conductivity, *i.e.*, the ease with which the impulse of con-

traction passes from one part of the muscle to the next, shows a tendency to diminution, especially with larger doses. This change appears to be related, however, at least in some cases, to the second fundamental effect of digitalis, *viz.*, that of stimulating the vagal cardioinhibitory apparatus, both centrally (in the medulla) and peripherally (in the heart). The third circulatory action of the drug, scarcely less important than the first two, is that on the blood-vessels, which, with certain significant exceptions, are caused to contract, both through stimulation of the vasoconstrictor center and a direct stimulating action on the walls of the smaller vessels.

The functional effects produced by digitalis are due to the simultaneous operation of the three factors just mentioned, which tend respectively, to increase the force of the heart beat, to slow the cardiac rate, and to raise the blood-pressure. With very small doses of digitalis, the effects may be exclusively those of the first factor, the heart muscle being mildly stimulated, but the rate unmodified except in certain susceptible individuals, in whom it may be actually increased. With somewhat larger doses the characteristic "therapeutic action" of digitalis appears,—a product of the combined muscular and vagal effects. In this condition the heart undergoes a greater degree of expansion during diastole, contracts more completely at each systole, and shows a diminished rate. The pulse wave is consequently much larger. Notwithstanding the slowing due to the vagal factor, the amount of blood delivered from the heart into the aorta in a given period of time may be increased. In abnormally dilated hearts, which al-

ready contain an excess of blood, digitalis lessens the capacity of the heart owing to the great improvement in tone it produces: but this does not exclude an increase of output, for the process of evacuation during systole is far more perfect than before.

The members of the digitalis series produce an acceleration of the blood-stream, followed by a retardation which appears under larger doses of the drug. In the greater circulation the peripheral stream is accelerated, while in the portal area there may be a similar effect if these vessels are not strongly contracted (Edmunds (Amer. Jour. of Physiol., Feb., 1907)).

'Strengthening of cardiac action is the dominant effect of digitalis. Through the increased systolic vigor, it causes a more perfect emptying of the ventricle, while by lengthening the diastole the heart action is slowed. The heart does not acquire muscular strength, but it utilizes more completely what strength it has, owing to the greater supply of blood the digitalis procures. Hirsch (Deutsch. med. Woch., Sept. 7 and 21, 1923).

That the diminution of cardiac rate caused by digitalis is chiefly due to vagal stimulation is shown by the fact that when the vagi have been completely paralyzed beforehand by means of atropine, which acts on the vagus terminals in the heart, the latter is not slowed by digitalis, but usually accelerated. If, instead of atropine, mere section of the pneumogastrics be practised, however, slowing still occurs (to a variable extent) after the administration of digitalis.

Digitalis does not slow the pulse through any direct action in patients with a normal heart rhythm. The writer's patients of this type improved impressively under digitalis, but did not show any slowing until they got better. Patients with an increased pulse rate showed slowing if there was

improvement otherwise, but only after the improvement occurred. In adults a reduction of rate should not be an object of digitalis therapy if the rhythm is normal. Digitalis in excessive dosage may produce *ventricular acceleration* either where there is normal rhythm or where there is auricular fibrillation. When a patient receiving digitalis in adequate amounts exhibits a definite acceleration in ventricular rate, the drug should be stopped. Luten (Ann. of Clin. Med., Sept., 1924).

Briefly, under ordinary conditions, the cardioinhibitory stimulation is exerted not only in the medulla, but in the heart itself. In the frog, atropinization does not prevent digitalis from slowing the cardiac rate (Böhm); conditions are, therefore, somewhat different from those existing in the mammal.

The slowing of the normal heart rhythm under digitalis is generally, but not invariably, inhibitory in origin. The slowing in auricular fibrillation does not arise from stimulation of the inhibitory center; in fact the inhibition is less active during the slow pulse than before or after the digitalis action. Experiments do not encourage the belief that the slowing of the pulse in this irregularity is due to failure in the passage of impulses through the auriculoventricular bundle. The heart in these cases is rapid, partly, perhaps, because it is irritable; it is half-starved, and the digitalis, by improving the contraction, may do something by way of improving the nutrition, and thus making the ventricle indirectly less excitable and less receptive for auricular impulses. Cushny (Proceed. Royal Soc. of Med., July, 1912).

The influence of digitalis on the T-wave of the human electrocardiogram may be detected in 36 to 48 hours after the use of digitalis was begun; it may persist as long as 22 days after its use has been stopped, though it may persist only 5. Cohn, Fraser and Jamieson (Jour. of Exper. Med., June, 1915).

A personal research confirmed the three-fold action of digitalis: 1, a paralyzing action on impulse center; 2, a paralyzing action on conduction mechanism; 3, a stimulating ventricular action. Maeda and Nakazawa (*Tohoku Jour. of Exp. Med.*, Apr. 30, 1922).

Both systole and diastole are lengthened when the heart is slowed by digitalis; the difference is more marked, however, in the latter than in the former portion of the cardiac cycle, the result being that the total period of diastolic rest experienced by the heart in a given time is increased at the expense of that of systolic activity—a condition highly favorable to improved cardiac nutrition.

The blood-pressure often shows little or no change after small or even moderate doses of digitalis in the normal human subject. Favoring a rise in blood-pressure are: (1) The increased output of blood from the heart. (2) Contraction of the vessels. The first of these factors is the resultant of two opposed conditions, viz., the increased amplitude of the individual beats and the lowered rate. If these are exactly equivalent, as appears frequently to be the case, the efficacy of this factor will be annulled. Furthermore, if an increased output of blood does, indeed, occur, other changes may indirectly take place which will counteract any effect this might have on the blood-pressure.

In normal animals digitalis has little if any influence on the blood-pressure, but it has a marked influence in raising the pressure in the isolated heart, especially when it was working badly before. Experiences in human beings practically confirmed these findings; as a rule the increase is insignificant and there may be even a drop in the pressure. The experiments that have been pub-

lished showing a vasoconstrictor action were with doses too large to be used therapeutically. With smaller doses, digitalis has a vasodilating action. D. T. Hernando (*Med. Ibera*, Jan. 24, 1918).

As suggested by Cushny, variations in the amount of blood supplied to the vasoconstrictor center induce variations in its activity in response to the blood requirements of the tissues in general. Where more blood is supplied to the center, as would be the case were digitalis increasing the cardiac output, the center would not be called on as much to maintain tone in the peripheral vessels, and, the walls of these relaxing, a tendency to a general reduction in blood-pressure would be present. Another factor that may be operative in preventing a rise of blood-pressure, and which may, indeed, cause an actual fall, is, in the presence of heart disease with stasis, the removal of the excess of carbon dioxide in the blood which is effected through the improved circulatory condition brought about by digitalis. Carbon dioxide, as in asphyxia, stimulates the vasoconstrictor mechanism and raises the blood-pressure; hence when the excess is removed, the proportion in the blood sinking to normal, the blood-pressure falls. According to A. W. Meyer, of Heidelberg, a reduction in the blood-pressure, previously abnormally high owing to stasis, has frequently been observed after the administration of digitalis. A rise in pressure due to the drug was, on the other hand, witnessed in but few cases by this author.

Strophanthus is often said to have less tendency to raise the blood-pressure than digitalis, but in patients neither induces any rise of pressure, and in some individuals,

the two cause an equal fall. There is, on the whole, rather less tendency to headaches, nausea and vomiting under strophanthus and squills than under digitalis, but the difference is not very marked and headache is caused in some cases by all three. Slight diarrhoea has followed the use of squills more than the others, and strophanthus also tends to cause this more than digitalis. This tendency to diarrhoea is still more marked from the use of helleborein and apocynum. A. R. Cushny (*Amer. Jour. Med. Sci.*, April, 1911).

Digitalin, even in full doses, does not affect the blood-pressure, except in cases with myocardial weakness, where the pressure is raised to its previous level owing to the beneficial effect of the drug on the heart muscle. One should not hesitate to use digitalin in cases with arterial hypertension. Josué and Godlewski (*Société méd. des hôpitaux; Semaine méd.*, Nov. 13, 1912).

The physician need not be afraid to give the drug in cases of **aneurism** on account of any danger of increasing arterial tension. Norris (*Penna. Med. Jour.*, Nov., 1912).

Prolonged observations in 32 cases has convinced the writer that digitalis never raises, but often lowers, the blood-pressure. Its hypotensor action seems to be more marked if a suitable dose of physostigmine has previously been administered. Danielopolu, of Bucharest (*Presse méd.*, June 5, 1916).

An analysis of the results, taking 14 cases together, shows that the administration of large doses of digitalis or digitoxin has very little tendency to elevate the systolic pressure, this having been increased by 11 mm. of mercury in one and 15 mm. in a second case. In only 1 case was the systolic pressure materially reduced, and in that instance by 23 mm. of mercury. On the other hand the diastolic pressure was significantly lowered in 7, or 50 per cent. of the cases, while it was never significantly raised. Digitalis and digi-

toxin have very little influence on the systolic pressure in either direction, and they tend to produce a significant reduction in the diastolic and, more decidedly, to produce a material increase in the pulse pressure. Cary Eggleston (*Jour. Amer. Med. Assoc.*, Sept. 22, 1917).

Of considerable importance from the standpoint of therapeutics are the changes produced by digitalis in the distribution of the blood in the body. Not only is the blood that has accumulated in the venous side of the circulation transferred to the arterial side—owing, at least in part, to the restoration of efficiency in the right ventricle—but there is now known to occur a special constriction of the intestinal and hepatic (including the portal) vessels, which serves both to remove congestion in these organs and to displace the blood into other parts. The intestinal vessels are the first to be constricted. The renal vessels, on the other hand, have been shown by Loewi and Jonescu to be actively dilated by small doses of digitalis.

Before passing on to the toxic effects of digitalis, it is necessary to mention a fourth action of the drug which is of some significance in its therapeutic use, viz., a regularization of the cardiac rhythm when the organ is not beating regularly. This effect is obtained only with therapeutic doses. Larger amounts tend, on the contrary, to bring on arrhythmia where it had not previously been present.

With toxic doses of digitalis, two additional series of effects are superimposed upon those already referred to. The first of these, the so-called second stage of digitalis action, is characterized essentially by a further



decrease in the cardiac rate and further vasoconstriction. The heart is so greatly slowed that the output of blood, notwithstanding the fullness of the individual beats, falls below that of the therapeutic stage, and even below that which existed before the drug was taken. The blood-pressure is distinctly increased, at least in the first portion of this stage. Irregularities of rhythm soon after appear, however, and the blood-pressure gradually tends to fall. The arrhythmia appears to be in part due to diminished conductivity in the cardiac tissues, including the bundle of His, which may lead to a lack of synchrony in the beats of the auricles and ventricles. Again, the auricles are believed to contract less strongly than before, and resulting abnormalities in the filling of the ventricles during diastole may account in part for the arrhythmia witnessed. That the vagal mechanism actually is in an extreme state of excitation is shown by the fact that if its terminals be paralyzed by an injection of atropine, the phenomena of the second stage are removed.

In the third stage of the action of digitalis, however, characterized essentially by an acceleration of the heart action, further irregularity and a more or less gradual fall in the blood-pressure, the direct exciting effect of digitalis upon the heart muscle figures more prominently in the phenomena witnessed. The vagal influence is no longer able to exert any effectual control over the ventricular contractions, which run riot and escape all efforts made to maintain proper auriculoventricular co-ordination. As a result, the efficiency of the heart as a pump is rapidly

lessened, and the blood-pressure falls. The condition present in the terminal phase is sometimes termed "delirium cordis." Not only is the rhythm markedly disturbed, but relaxation of the heart in diastole takes place with increasing difficulty, owing to the excessive and progressively augmenting tone of the heart muscle caused by the drug. The final result is complete arrest of ventricular activity; the circulation ceases with the ventricles in the systolic position, but in mammals the ventricular walls immediately relax, so that the usual position of permanent arrest is semidiastole. Not infrequently, in guinea-pigs at least, the auricles continue to beat at a fairly high rate for a number of minutes after ventricular arrest.

In the frog, the typical position of cardiac stoppage is that of systole, the ventricle remaining firmly contracted and pale. It is of interest to note that certain non-vegetable substances, in particular barium salts and bufalin, a glucosid obtained from the skin of certain species of toad, have the same property of causing arrest of the frog's heart in permanent systole.

*Respiration.*—The direct effects of digitalis on the respiratory center are of no importance from the therapeutic standpoint. Respiration is rendered easier in cases of heart disease indirectly through the improvement in the blood-circulation. With toxic doses, however, the respiratory center appears to share to a certain extent the stimulating effect of digitalis on the vomiting center. At an advanced stage in digitalis poisoning in animals there is sometimes seen a sudden marked increase in the rate and depth of breathing, which, on some occasions at least, appears to correspond

to the beginning of poor circulation owing to the toxic action of the drug on the heart muscle. There appear, thus, to be two ways in which the respiratory center may be stimulated: first, directly by the drug, and, second, indirectly owing to the excess of carbon dioxide present as the result of impaired circulation. At the close of poisoning the respiration often becomes slow and shallow; this may be due either to secondary depression of the nervous mechanism of respiration by the drug itself or to the poor supply of blood reaching the centers by reason of the increasing circulatory inefficiency.

*Kidneys.*—In normal individuals digitalis has only a slight effect on the secretion of urine, but in the presence of heart disease it acts as a powerful diuretic. The drug is not believed to exert a direct stimulating effect upon the renal epithelium and, in fact, no such action is necessary to explain the results produced. In heart cases it acts by improving the circulation. Not only does more blood pass through the kidneys in a given time, the function of these organs being thereby activated, but, owing to diminished venous congestion, the flow of lymph into the blood-circulation,—*e.g.*, from the thoracic duct—is facilitated, effusions being thus drained and the blood rendered hydremic, a condition favoring diuresis.

Until comparatively recent times, the preceding statements would have represented a complete explanation, in so far as was possible, of the diuretic action of digitalis. A feature remaining obscure, however, was the reason why, if the activity of the kidneys is so greatly increased, the functions of various other structures

concerned with the elaboration of fluids are not similarly enhanced by digitalis. In 1908 this gap in our knowledge of the drug's action was filled through the investigations of Jonescu and Loewi, who showed that small amounts of digitalis bodies caused an active dilatation of the renal vessels, while the blood-pressure remained the same as before or was very slightly raised. The authors attribute the vasodilator effect in the kidney to direct excitation of the terminals of the renal nerves. When to this action of digitalis are added the improvement in the general circulation, the reabsorption of edematous fluid with resulting hydremia, and the displacement of blood from the intestinal walls and liver by virtue of the vasoconstrictor effect digitalis is known to exert in these parts, it will be seen that several factors co-operate in the diuretic action of digitalis.

The diuretic effects of digitalis may be produced with no perceptible change in the heart. Mackenzie (*Heart*, vol. ii, 273, 1911).

The diuresis induced by digitalis is the result both of a stimulating action on the heart, manifested in an increase of the pulse pressure—*i.e.*, of the difference between the systolic and diastolic pressures—and of a vasodilator action in the kidneys, most clearly indicated by a diminution in the diastolic pressure. The drug is thus both indirectly and directly diuretic. Digitalis tends to cause an increase of the viscosity of the blood; this, after the resorption of edema, tends automatically to check diuresis, which might otherwise become excessive. Martinet (*Presse méd.*, Oct. 5, 1912).

Another fact to be remembered is that where the amount of digitalis in the system exceeds a certain limit, the renal vasodilatation gives way to con-

striction. Notwithstanding the persistence of the other factors favoring diuresis, the latter then becomes impossible because the blood-supply to the kidneys is subnormal. The only course remaining under these conditions is to stop the drug and wait until a portion of that in the organism has been destroyed or eliminated, when diuresis will reappear.

The diuresis produced by digitalis in ordinary doses of the pharmacopeial preparations does not make its appearance before the third or fourth day of administration. When digitalis fails to produce diuresis in **cardiac dropsy** the use of it is not to be abandoned, but it is to be given in larger doses. [Not always.—*Ed.*] Digitalis which is acting or has acted as a diuretic in cardiac failure must not be suddenly taken away, and must be slowly, not rapidly, reduced in dose before its final removal. Measuring the volume of urine is a ready, accurate, and sufficient index both of the patient's condition and progress. J. Mitchell Bruce (*Brit. Med. Jour.*, Jan. 6, 1906).

A man aged 52, with an old double mitral affection, pulsation in the jugular and auricles, and a radial pulse of 40 of very low tension, developed, in process of time, **dropsy** of the legs with scanty urine. Rest in bed for a week had failed to remove the dropsy, and at 9 one evening he was given 15 minims (1 c.c.) of tincture of digitalis of known potency. By 5 next morning diuresis had set in and was kept up by small doses of the drug till the dropsy had cleared away. This was an unusual experience in that the drug acted more rapidly than it is generally believed to do. Gordon Sharp (*The Antiseptic*, July, 1908).

**Temperature.**—In large doses digitalis tends to lower the temperature where fever is present. The cause of this is not known. The property is of little practical use, for wherever temperature is lowered in the presence of

digitalis the vagal inhibitory effect of the drug on the heart, which is interfered with by fever, asserts itself in marked degree, with the result that a dangerous amount of slowing of the heart rate may occur. Since large doses of digitalis are already required to lower the temperature, the futility of using the drug for antipyretic purposes is evident. According to some, the antipyretic effect of digitalis is preceded by a transient rise in temperature.

**Metabolism.**—Digitalis does not appear to exert any direct effect on tissue metabolism, though general nutrition, and in particular that of the heart muscle, may be improved through its continued effect. Where the drug is given in the presence of edema due to circulatory weakness, a pronounced discharge of chlorides and urea takes place in the urine, but this represents merely a relief from the preceding retention of these substances in the tissues at large.

From a study of 12 cases the author concluded that there is a marked leucocytosis after the use of digalen. The increase regularly occurred from 7 to 8 hours after the injection of digalen, and there was reached within 24 hours double the original number of leucocytes counted. The leucocytosis recurs whenever digalen is administered. Mirano (*Riforma Medica*, June 8, 1907).

A comprehensive research showed that digitalis activates the secretory functions of the kidneys, stomach, pancreas, and thyroid. Veil and Heilmeyer (*Deutsch. Arch. f. klin. Med.*, Apr., 1925).

**Absorption and Elimination.**—Digitalis is slowly absorbed, and even when absorbed is slow, it is said, in exerting its effects on the heart. The galenical preparations of digitalis, when taken internally, do not begin to

take effect, as a rule, for some hours, and the maximum effect of full doses on the heart is not obtained for forty-eight hours or even, according to the curves published by Eggleston, about three days. This does not mean, of course, that a useful therapeutic effect cannot be obtained before this period has elapsed. Some delay appears to occur, however, in the combination of the active substances of the drug with the heart muscle; from this, as well as from the slower rate of absorption into the blood, arises the difference between digitalis and strophanthus in rapidity of effect.

The effect of the digestive secretions on digitalis taken by the mouth has been shown to have a definite bearing on the proportion of the drug absorbed.

Worth Hale has ascertained by experiments *in vitro* that an artificial gastric juice caused deterioration of the various individual glucosids, as well as of the tincture of digitalis, amounting to about 25 to 35 per cent. in three hours. Believing that certain of the untoward effects seen in digitalis medication may be due to the decomposition products of the glucosids, and in view of the fact that the deterioration was shown to be due chiefly to the hydrochloric acid in the gastric juice, he advises that an alkali be prescribed with digitalis.

Digitoxin, the most important principle in digitalis, is absorbed from the intestines and not the stomach. The absorption is a relatively slow process, usually not completed before five to six hours; this absorption is still further delayed where there is stasis in the portal circulation. Digitoxin is much more rapidly absorbed from digipuratum than from the powdered leaves. R. Gottlieb and S. Ogawa (Münch. med. Woch., Oct. 22, 1912).

In a series of over 200 experiments, the writer found that the rate of digitalis elimination varied with different specimens, from 74.5 per cent. in 22 days to 92.9 per cent. in 4 days in this series; the persistence of one specimen may be several times that of another. Moreover, the digitalis bodies can produce an effect that persists independently, to a degree, of the presence of the drug. Digitoxin produces an effect that for a short time increases in intensity, while the rapidly eliminated fraction does not exhibit this rising effect. The persistence of digitoxin as tested by the method of repeated dosage is considerably longer than that of the ordinary tinctures of digitalis. The curve of digitalis elimination is complex and variable, depending on the resultant action of the rapidly eliminated and the digitoxin-like fractions. Repeated doses sensitize to later action of the drug. H. Gold (Arch. of Intern. Med., Nov., 1923).

The fate of the digitalis substances in the system is not definitely known. It appears very likely, however, that, at least in part, they become rather firmly fixed in the tissues, especially the heart muscle. Attempts to detect the principles in the urine have met with but little success; it seems probable, therefore, that these substances are for the most part gradually destroyed in the system.

The slowness with which the effects of digitalis disappear is a matter of common observation. This is believed to be due to an actual persistence of the drug in the body and not to continuance of the effect after its destruction or excretion. As Hatcher and Eggleston showed in 1912, there remains in the tissues after the total disappearance of all signs of the action of digitalis, a large portion of the whole amount absorbed before the administration of the drug had been stopped. That this residual portion,

moreover, is not actually present in an inert state, but in what may be termed a potentially active condition, is proven by the fact that if doses smaller than those previously used are given at varying intervals of time after the initial discontinuance of the drug, physiological effects similar to those first noted from the larger doses reappear, *i.e.*, there is a summation of the effects of the added small amounts with potential effects of the amounts previously fixed in the tissues. Thus, in one of Eggleston's cases in which coupled beats had been induced by 3.25 Gm. (50 grains) of digitalis leaf taken in a period of seven days, and persisted for nine days after cessation of the drug, 0.675 Gm. (10½ grains) then given caused the coupled beats to reappear in two days, *i.e.*, eleven days after the last dose of the first course of treatment; during this entire period, furthermore, destruction or elimination of the drug had presumably been taking place. The period following the initial discontinuance in which no digitalis effect can be shown present by means of tracings or even, in the majority of cases, by clinical signs, has been termed by Hatcher and Eggleston that of the "latent action" of digitalis. The possibility of summation of the effects of doses given at relatively long intervals is a factor in the so-called "cumulative action" of digitalis.

Persistence of digitalis action is due, not to the lasting effects of an injury to the heart, but to the actual presence of the drug in the tissues in active form. Experiments with ouabain showed a much higher and more intense action at once, with more rapid elimination, than was the case with digitalis. Cary Eggleston (Jour. Amer. Med. Assoc., Oct. 12. 1912).

It has been shown in animals that the destruction or elimination of digitalis occurs more slowly when the dose given is very toxic than when it is small. Judging from the clinical experiences of Eggleston this would appear to be true also in man. This observer found that after the administration of doses large enough to bring on untoward signs such as partial heart block and coupled beats, these conditions persisted for three to twelve days after the drug had been stopped. The slow elimination of even relatively small amounts of digitalis was illustrated in the experiments of Marvin, who gave a single dose of 20 minims (1.25 c.c.) of tincture of digitalis to each of 20 men and observed a rise in blood-pressure which reached its height in twenty-four hours and did not finally disappear until after fifty hours.

**UNTOWARD EFFECTS AND POISONING.**—The untoward effects of digitalis most frequently met with are those representing the so-called "cumulative action" of digitalis. This is defined by Eggleston as "the development under small repeated doses of a drug of symptoms which are much more marked than those caused by a single dose." The condition is essentially one of poisoning in mild degree, and in some instances is characterized by the fact that the unfavorable effects develop entirely without warning, at a time when no action beyond the therapeutic is expected. The cause of cumulation is an excess of intake over outgo or destruction, and its prominence in the case of digitalis seems to be wholly accounted for by the slowness with which the system gets rid of the drug as compared to the elimination of other

agents of the same group, *e.g.*, strophanthus. A portion of every dose ingested, even though the latter be small, becoming rather firmly fixed in the tissues, including probably those of the heart itself, a time soon comes when the added effects of the amounts successively fixed surpass the therapeutic level, and symptoms of poisoning therefore occur. The only feature remaining, perhaps, unexplained by the above facts is the suddenness with which these effects occasionally appear. It seems not unlikely that this may be the result, at least in certain cases, of the intervention of other factors, such as: (1) Diminished elimination, owing to deficient renal action; lessening in the amount of urine excreted is itself not infrequently an associated sign of cumulative action, the amount of digitalis present in the body having become so large as to induce renal vasoconstriction, an effect hindering diuresis. (2) More rapid absorption of several doses from the alimentary canal owing to some local condition (temporary active hyperemia, or improved circulation, favoring absorption) not previously present. By the co-operation of one or more factors such as these with the slow destruction of digitalis in general, an increased degree of suddenness in the onset of toxic symptoms may obviously be the result. That variations in the rapidity of absorption from the alimentary canal do not account wholly for "cumulative action" is shown by the fact that the latter occurs even upon exclusively intravenous use of the drug.

In a study of 24 specimens of American digitalis, both wild and cultivated, from different parts of

the Union, by the writer, 6 were found to be above the U. S. P. standard, 3 were exactly of standard strength, and 15 were below it. Pratt (Pharm. Jour., Sept. 14, 1918).

The emetic action of digitalis is exerted as a reflex from the direct action on the heart, the afferent impulses passing to the vomiting center in the medulla by way of the sympathetic mainly, and probably in part by way of the vagus. Hatcher and Weiss (Arch. of Int. Med., May, 1922).

The signs and symptoms resulting from an excessive amount of digitalis in the body are referable both to the heart itself and to a number of other structures.

Nausea and digestive disturbances are generally among the earliest phenomena to appear. They have usually been ascribed to direct irritation of the stomach by the drug, and, as a matter of fact, the digitalis glucosids do irritate the mucous membranes. Recent researches have indicated rather clearly, however, that the nausea may be due to irritation of the vomiting center in the medulla, and that, in the lower animals at least, an amount of the drug bearing a certain definite ratio to the lethal dose will regularly bring on centric vomiting. That the fatty substances in digitalis are probably not in any large degree responsible for gastric disturbances is suggested by an experiment of Eggleston and Hatcher, who fed about 2 grains (0.13 Gm.) of the fixed oil of digitalis—an amount corresponding to 70,000 therapeutic doses of the tincture—to a cat without gastric or other symptoms resulting.

Usually the first symptom complained of is nausea, and later vomiting, though at times severe headache is the first and chief complaint. There is frequently a feeling of

malaise, with weakness and giddiness on standing, which, added to the anorexia and nausea, give a symptom-complex frequently likened by patients to seasickness. Diarrhea is occasionally produced, but less often by digitalis than by the other members of the group.

Rarely digitalis produces mental symptoms, confusion, loss of memory, hallucinations, and at times transient aphasic attacks.

Diarrhea, if it be present, may not subside at once when the drug is stopped and may require the administration of a dose or two of **castor oil**, preferably combined with **opium**. H. Hume Turnbull (*Austral. Med. Jour.*, Oct. 19, 1912).

Where vomiting or nausea occurs after digitalis, there may be one of two causes. The principles in the drug may directly irritate the stomach; in such cases the distress is noticed early, even after relatively small doses, and is usually accompanied by salivation (in cats). The digitoxin is generally still in the stomach and has not been absorbed. Or, the vomiting may be a true toxic effect of the drug seen after an excess has been given. Here general symptoms from absorption usually appear after six to seven hours. At this time no digitoxin is found in the stomach. R. Gottlieb and S. Ogawa (*Munchener med. Woch.*, Oct. 22, 1912).

The vomiting from digitalis is due almost entirely to the direct action on the vomiting center in the medulla. In the author's experimental investigation the smallest amount of any digitalis body that was followed by emesis was about 20 per cent. of the fatal dose, in the case of true digitalin. Of 61 animals receiving more than 30 per cent. of the fatal dose, 41 vomited, and it was remarkable that of the non-proprietary bodies the drug showing the greatest emetic activity was that which is generally supposed to be the least irritating to the stomach, *vis.*, true digitalin. Action on the vomiting center cannot be removed from any of the digitalis bodies by any process of

purification. Only traces of digitonin are found in the galenical preparations, and they exert no appreciable effect on the stomach after giving therapeutic doses.

The administration of opium to prevent the gastrointestinal symptoms of the digitalis bodies, in ordinary cases, masks the appearance of toxic symptoms which should serve as a signal for reduction of the dose.

The results of the investigations by the writers lent no support to the claims that digalen, digipuratum, digitalysatum or the fat-free tincture of digitalis are less actively nauseant or emetic in proportion to cardiac activity than galenical preparations. C. Eggleston and R. A. Hatcher (*Jour. Amer. Med. Assoc.*, Feb. 15, 1913).

The errors in the use of digitalis may be grouped together in 6 classes: 1, Prescribing digitalis in nervous disorders of the heart; 2, it is often prescribed in doses too large; 3, sometimes the physician waits to prescribe it until symptoms of myocardial heart-block have reappeared; 4, the drug is stopped when the heart has recovered its contractility; 5, success is expected from large doses when small doses have failed; 6, small doses are prescribed for too long a time. It is under the conditions of 4, as the writer points out, that most of the clinical accidents, often fatal ones, have occurred. Fiessinger (*Rev. gén. de clinique et de thérapeutique*, vol. xxx, p. 536, 1916).

A decrease in the amount of urine passed, or actual suppression, is another frequent and more definite sign of digitalis intoxication. It shows that enough of the drug is present to substitute for the renal vasodilatation caused by small doses a pronounced vasoconstriction, which tends to arrest the renal function. When oliguria appears, digitalis should be discontinued, or, at least, the amount greatly reduced, for this condition may lead to further impairment of

digitalis elimination and thus accentuate the toxic effects. Occasionally signs of renal irritation, such as albuminuria, occur in conjunction with oliguria under digitalis.

Headache, with a sensation of "tightness" in the head, and numbness ("emptiness") or coldness in one or more extremities also occur as evidences of digitalis poisoning. They are probably due chiefly to changes in the caliber of the vessels, particularly vasoconstriction.

Dizziness, nightmares, mental confusion, and anemia are likewise not infrequently caused by digitalis. Robertson has seen several maniacal outbreaks follow the use of this drug.

Some nocturnal delirium is one of the bad results of digitalis. Pallor, coldness of the extremities, trembling, and contraction of the pupils, are important indications to suspend the drug. Some patients die suddenly of syncope, others gradually. Death from digitalis is most frequently met with in Bright's disease, arthritic and anemic subjects, and in persons with aortic incompetence or delirium tremens.

Occasionally there is melancholia and night-terrors. An unusual result is pulmonary apoplexy. Potain (*Jour. de méd.*, April 10, 1900).

In an experiment on 20 female Belgian hares, which tended to show that large doses of digitalis, continuously administered, will cause slight enlargement of the normal heart, the development of a vicious and carnivorous tendency among the animals which took the digitalis was an interesting feature of the experiment. The animals were at first very docile. As the dosage of the remedy increased they began fighting and biting each other in a most ferocious manner. The two experimental animals which died were found in the morning mutilated and in part devoured. The control animals remained docile. F. B. Wynn (*Jour. Amer. Med. Assoc.*, July 16, 1904).

A number of cases have been noted where what was called delirium tremens was found after a time to result from digitalis. Its removal was followed by subsidence of symptoms. This is apt to occur in persons of unstable mental and emotional states. Hall (*Quarterly Jour. of Inebriety*, Oct., 1905).

Case of a woman with angina pectoris and chronic myocarditis who developed attacks of yellow vision while taking tincture of digitalis, 15 minims *t. i. d.* Jackson and Zervas (*Boston Med. and Surg. Jour.*, May 7, 1925).

As regards the heart itself, the most evident signs of excessive digitalis action are pronounced slowing of the cardiac rate—below 55 or 60 beats per minute—palpitation, and a subjective feeling of oppression in the heart region. The slowing is frequently the result of excessive inhibition through the vagi. Various forms of irregularity have also been detected after digitalis. Eggleston classes these, in the order of increasing intensity, *i. e.*, from the effects of larger and larger amounts of digitalis, as follows: (1) Sinus arrhythmia, consisting of periodic waves of slowing involving the entire heart, with subsequent more or less rapid return to the normal rate. This phenomenon is considered due to vagus stimulation. (2) Muscular irritability, associated with the production of extrasystoles or abortive contractions, and due to the direct action of the drug on the myocardium. This disturbance is not as frequently seen as the result of digitalis action as the preceding disturbance. (3) Auricular fibrillation, *i. e.*, loss of co-ordinate contraction in the auricle and its replacement by the formation of independent contractile impulses at numerous points, was brought on by digitalis in a previously regular heart in a case reported by Mackenzie. (4)



Combined phenomena,—*e.g.*, extra-systoles, heart block, and sinus arrhythmia. (5) Heart block, partial or even complete, an expression of the effect of digitalis in lowering the conductivity of the auriculoventricular bundle of His, and manifested by a prolongation of the interval between the auricular and ventricular systoles, in more severe grades by the complete omission of some of the ventricular beats, and in the "complete" form by continuous dissociation between the auricular and ventricular rates, the two portions of the heart beating independently. According to Lewis, the severer grades of partial heart block are not infrequently observed when digitalis or its allies are given in toxic doses to young patients with rheumatic hearts. (6) Coupled beats, the most serious of the untoward actions of digitalis on the heart rhythm. The successive pairs of beats can sometimes be felt at the wrist. This condition is said to occur only in hearts the seat of auricular fibrillation. The minimal amount of digitalis that can produce coupled beats in cases of auricular fibrillation is, according to Eggleston's experience, 2.25 Gm. (34 grains) of the leaves.

Of the various cardiac irregularities produced experimentally by digitalis, the earliest to appear in most instances is an occasional omission of ventricular contractions, owing to an interruption of the stimulus between the auricles and ventricles. Somewhat later, or even immediately after this, the heart may assume a peculiar rhythm in which the auricles and ventricles are beating quite independently of each other. This irregularity differs from the ordinary rhythm of complete heart block in that the ventricular rate is not slow, but approaches and usually exceeds the

auricular rate; so that, for example, one may count 16 ventricular to 15 auricular contractions. This rhythm is common in carefully graded digitalis poisoning in dogs, but had never been described in man until the author's report of a case. The venous tracings taken one day before this patient died showed a regularly recurring cycle of changes. Each cycle required about seven seconds for its completion, and included about 14 ventricular contractions. At certain portions of the cycle, a single, sharp, positive wave occurred in the jugular pulse just after the onset of ventricular systole. Midway between these groups of sharp waves, each ventricular systole was represented on the venous pulse by two waves of almost equal height connected by a more or less distinct plateau. These cycles, from their duration, were evidently independent of the respiration, for the respiratory rate was constantly about 30 a minute. It was found that the patient had been taking drugs of the digitalis series in considerable quantities for a long period. During all this time his heart-failure was gradually becoming worse, although the daily amount of drugs taken did not seem excessive. At no time was marked slowing of the pulse observed. A. W. Hewlett (*Archives of Internal Medicine*, Feb., 1910).

Toxic effects of digitalis and related bodies may usually be discovered in their earliest stages by careful and frequent sphygmographic observations, and may be divided into three periods with regard to their occurrence and severity: (1) Period of vagus stimulation; (2) period of depression of conductivity with masked vagus action; (3) period of marked muscular irritability with depression of contractility. Muscular irritability may be the first symptom observed, the other stages being short in duration and easily overlooked. This irritability from digitalis must be differentiated from the progress of the cardiac disease by careful observations of combined jugular and radial tracings. With therapeutic doses the rise of blood-pressure due to vasoconstriction is so slight that it may be disregarded,

but with toxic doses it becomes of extreme importance. H. C. Bailey (*Amer. Jour. Med. Sci.*, Aug., 1911).

Eggleston and Wyckoff have recommended, in prescribing digitalis, a dosage equivalent to 1 c.c. (15 minims) of the tincture or 0.1 Gm. ( $1\frac{1}{2}$  grains) of the leaf for each 10 pounds of the patient's body weight. As certain investigations have shown that the body disposes daily, on an average, of 22 minims of the tincture of digitalis of standard potency, it is necessary, when the administration of the drug is continued over a series of days, to subtract the amount disposed of in order to ascertain the total quantity of digitalis considered active in the patient at any one time.

The writer analyzed the records of 13 cases exhibiting untoward results, and in practically every instance a quantity of the drug in excess of the amount indicated by the Eggleston method of calculating had been administered. The toxic effects which followed included coupled rhythm, partial heart-block with an acceleration of the sinus rate, the onset of auricular fibrillation, and paroxysmal tachycardia originating in the ventricle. When using a large dosage of digitalis the physician should know at all times the relation of the amount of the drug already administered to that which would be expected to be the approximate amount for therapeutic effect. After the first few doses, the drug should not be administered more frequently than at 6-hour intervals, so that sufficient time may elapse to disclose the effect of the preceding dose before another is given. If signs or symptoms appear that may be due to toxic effects of the drug, and if calculation shows that the amount already given is near or above the Eggleston dosage, additional digitalis should only be administered cautiously, if at all. W. D. Reid (*Jour. Amer. Med. Assoc.*, Aug. 11, 1923).

Hewlett points out the fact that in young persons, in neurotic individuals, and after infectious diseases, the

controlling influence of the vagi on the heart is particularly marked and labile. Irregularities associated with excessive vagal action are, therefore, especially likely to result from the use of digitalis in these cases.

Acute poisoning by single massive doses of digitalis is infrequent. The earliest symptoms are nausea and vomiting, the latter violent and repeated, together with headache, dizziness, and visual disturbances. The pulse for a time is rendered slow and powerful, but later tends to become feeble and irregular, and is accelerated when the victim leaves the recumbent posture. Vasomotor changes and altered distribution of blood in the body are betokened by pallor of the face, prominence of the eyeballs, and a blue color of the sclera. Diarrhea is likely to be observed; there may be salivation of central origin; the flow of urine may cease owing to renal vasoconstriction; there may be pain in the extremities or back, and in the later stages of the poisoning dyspnea is a prominent symptom. The body temperature is lowered; delirium may supervene, followed by stupor, and pronounced motor weakness or actual paralysis finally occurs, owing to a curare-like action on the motor nerve-endings. If paralysis is not complete, convulsions may develop. Death, if it takes place, occurs usually in one or two days. According to Wood, the limits in the duration of the poisoning are, respectively, three-quarters of an hour and ten days. Most cases of digitalis poisoning recover.

A boy 2 years old, one morning obtained a box containing granules of Nativelle's digitalin and swallowed five of them. Each one contained  $\frac{1}{250}$  grain (0.00026 Gm.). He remained well until evening, when he became unusually

cross; early the next morning he vomited repeatedly and became very drowsy. When seen he was semiconscious and pale; pupils somewhat dilated; vomiting small quantities of bile-stained mucus; sweating profusely; extremities were cold, pulse was so irregular and intermittent that it could not be counted, and the respirations were extremely shallow and slow. The patient was given 2 grains (0.13 Gm.) of **calomel** and liberal quantities of **brandy** and water. When seen again, about three hours later, the condition in general was much worse; the child was absolutely comatose. On the evening of the same day there was some improvement, and from that time on recovery was uninterrupted, though slow. Frank Radcliffe (Brit. Med. Jour., p. 338, 1901).

Preparations of digitalis which fail to produce nausea and vomiting when given in large doses are either weak or imperfectly absorbed. Robinson (Medicine, May, 1922).

*Treatment.*—In cumulative poisoning, withdrawal of the drug for some days is generally all that is required. In view of the fact that rising from recumbency to the upright position or exertion of any other kind by patients fully under the influence of digitalis places considerable added strain upon the heart, these cases should be kept as quiet as possible.

In poisoning from single toxic doses of digitalis **tannic acid** or **Lugol's solution** may be administered as antidote. The most important measure, however, is to secure evacuation of unabsorbed poison by **washing out the stomach** or, if necessary, giving **emetics**. The drug is, of course, likely itself to produce emesis. **Magnesium sulphate** should be given to prevent further absorption from the intestinal tract. **Moist, hot applications to the lumbar regions** have been recommended, to favor relaxation of

the constricted renal vessels and promote elimination of the drug through this channel. To overcome the general vasoconstriction, **nitroglycerin** or **alcoholic preparations** may be used. In the later stages of poisoning, depression of the medullary centers is an important source of danger; stimulants such as **caffeine** or **hot coffee**, **strychnine** and **atropine** should therefore be used. **Artificial respiration** should be instituted as soon as dyspnea appears, as it has been shown experimentally that life can sometimes be prolonged for hours in this way or even, occasionally, animals saved from a dose otherwise certainly fatal.

When in the frog the heart action had been arrested by toxic action from digalen, the heart could be resuscitated temporarily by the action of **hydrocyanic acid**. The reverse also occurs, digalen resuscitating the heart arrested with the hydrocyanic acid. Bastert (Nederl. Tijdsch. v. Geneesk., Nov. 9, 1919).

**THERAPEUTICS.—Diseases of the Heart.**—Digitalis is, on the whole, by far the most useful drug available for the treatment of cardiac disease. It is the typical representative of a group of drugs characterized not so much by their power to stimulate cardiac activity in acute conditions, although this, in itself, forms part of their field of usefulness, as by that of improving the nutrition of the myocardium where it is impoverished or where increased contractile activity is demanded to overcome mechanical obstacles, local or remote. These agents, with their slow-going and more or less persistent influence on the heart, are often termed "heart tonics" in contradistinction to "stimulants" such as ether, atropine, and alcohol, which temporarily reinforce

cardiac action chiefly in various indirect ways and do not necessarily leave the heart, after their immediate effect disappears, in a better nutritive condition than they found it.

The improvement in cardiac nutrition brought about by digitalis may be ascribed to several simultaneously operative factors. Thus, it is stated that the drug, through the prolonged exciting effect it exerts directly on the heart muscle, improves the coronary circulation by making the beats stronger, and thereby enhances its own blood-supply. Again, slowing of the heart rate through vagus stimulation tends to rest the heart by prolongation of the period of diastole, during which the organ recuperates from the preceding systole. It is a well-known fact that in the presence of rapid cardiac rates the diastolic period in each cardiac cycle is shorter in comparison with the period occupied by systole than is the case when the rate is slow; hence the total amount of rest obtained by the heart under digitalis is increased. According to Hering and Gaskell vagus stimulation also exerts a favorable trophic influence on the heart muscle, directly increasing the anabolic or building up processes in the cardiac tissues. Finally, a by no means inconsiderable factor in the improved nutritive state brought about by digitalis is the interruption of a vicious circle in which the heart's own weakness reacts on the quality of the blood supplied to it. The feebler the heart, the greater the impairment in the pulmonary, gastrointestinal, hepatic, and renal functions, through which the blood is maintained in its normal state of aëriative and nutritive efficiency, and low toxicity; the more

inadequate the blood itself, in turn, the greater the impairment in cardiac activity. By relieving venous congestion through increased cardiac power, and by bettering the distribution of blood through vasoconstriction in the splanchnic area, the renal vessels meanwhile remaining unconstricted, digitalis breaks into the vicious circle and, where conditions are not too serious, places the heart on the high-road to functional recovery.

All myocardial degenerative processes resulting in loss of circulatory equilibrium and culminating in cardiac failure can, in their incipency, be postponed if digalen is given and its administration continued as indications require. Later they may be controlled and the circulatory equilibrium maintained for many years longer with this agent than under other methods. H. Beates, Jr. (*Amer. Jour. Clin. Med.*, vol. ii, p. 1025, 1915).

The dangers of toxic effects as given in text-books are exaggerated. The real dangers in digitalis therapy are three: (a) Using a poor digitalis preparation. (b) Consciously or unconsciously prescribing too little of a potent digitalis preparation. (c) Not knowing when digitalis should be started and stopped. Digitalis usually is given in too small, *i.e.*, insufficient dosage. The large majority of cardiac patients seen had had too little digitalis; a small percentage had had enough digitalis; none had had too much; some should have had none. Digitalis poisoning, of course, is possible, but it is one of the rarities of medicine. Christian (*Boston Med. and Surg. Jour.*, July 13, 1922).

The above features by no means exhaust, however, the possibilities for good to be thought of in connection with this drug. Since the remaining factors differ according to the particular cardiac affection for which the drug is used, and, still more, because the indications for digitalis vary enor-

mously in the different states, the latter will now be considered *seriatim*.

**Cardiac dilatation** is perhaps the most direct indication of all for digitalis, since one of the prominent actions of the latter is to increase the tonicity of the heart muscle and hence overcome abnormal distention of this organ. In **simple acute dilatation**, such as results from excessive physical effort, the patient should at first be placed on small doses, the amount then being gradually increased until pronounced benefit is noted; absolute rest should, of course, be simultaneously imposed. In the acute cardiac dilatation of **infectious diseases**, digitalis is less striking in its effects, but is nevertheless frequently of value. Underlying the failure of cardiac power there is, of course, usually an **acute myocarditis**, with perhaps even fatty degeneration of the heart tissue. The more pronounced these myocardial changes, the less useful the drug is likely to prove and the greater the caution required in its employment, except in the final stage as an ultimate resort. As in simple dilatation from exertion, small doses, such as 1 or 2 drams (4 to 8 c.c.) of the infusion should be used at first, unless the phenomena of cardiovascular failure are very acute, when larger amounts may be given together with other stimulants. It is important, in giving digitalis in the course of infections, not to judge of the effects of the drug by a change in the pulse rate, *i.e.*, not to expect slowing, as vagal activity is diminished in fever; the quality of the heart sounds should rather be taken as criterion in regulating the dose. Calcium, in the form of the lactate or lime water, is to be thought of as a useful heart remedy,

and, in cases where free use of digitalis is deemed unsafe, should be tried without hesitation. Digitalis is not well suited for cases with pronounced nervous excitement. In **pneumonia** the value of digitalis as a heart tonic has been particularly emphasized, and even its administration throughout the disease advocated.

It is often stated that in **chronic myocarditis** or **cardiac fibrosis**, as well as in **fatty degeneration**, with signs of functional insufficiency of the organ, digitalis is of little or no value. The heart muscle, having been weakened through partial replacement by non-contractile tissue, is said not to be able to respond to the stimulating effect of digitalis and in some instances to be injured rather than benefited by the drug. The alleged effect of digitalis in raising the blood-pressure has also been advanced as a reason for withholding digitalis in these cases, on the ground that undue resistance to the heart action is imposed. It has of late become evident, however, that digitalis, except in a few instances, has little or no effect on the blood-pressure, which may, in fact, be somewhat reduced. Many clinicians, moreover, advise its use. Thus Abrahams states: "Patients with myocarditis can stand 15-drop doses of the tincture three times a day very nicely. It does them a great deal of good." In view of these facts, it would appear that the dangers attending the use of digitalis in chronic myocarditis have been overdrawn, and that with due caution as to dosage, more particularly where there is reason to suspect pronounced fatty changes, there should be little hesitation in employing the drug. By some *strophanthus* is given preference over

digitalis in these cases, with the idea that the vessels are less constricted by the former than the latter. There is reason to believe, however, that too much stress has been laid on this difference between the drugs. Where it seems especially desirable to avoid any increase of blood-pressure, nitrites may be given with the digitalis (preferably at shorter intervals, since their effect is of brief duration).

In **myocardial degeneration** from any cause, the writer notes both the apical and pulse rates at the time the patient is put to bed. If no slowing of the rates occurs, and no lessening of the tendency to abortive systoles takes place, as evidenced by the discrepancy between apical and pulse rate, in the majority of the cases one will find that digitalis cannot be used at all, or, if used, is disappointing in its effects. W. E. Robertson (Penna. Med. Jour., Nov., 1912).

The indications for starting digitalis therapy are the presence of symptoms and physical signs which are the result of cardiac inefficiency. These are breathlessness, cough, cyanosis, edema, pain, weakness, nausea, vomiting, enlargement of the liver, decreased urine output, rapid pulse. The indications for stopping digitalis are improvement in these symptoms and signs or the occurrence of some of the toxic effects of digitalis. The latter are nausea, vomiting, certain arrhythmias, as bigeminal pulse and heart-block, rarely diarrhea. Very often digitalis has but slight potency. A serious error is to regard a drop as a minim and to prescribe 15 drops of tincture of digitalis, thinking to give 15 minims; the patient taking 15 drops often gets but 5 minims, rarely more than 7 minims—both very small doses. This accounts for much unconscious prescribing of too small a dose. Definite evidences of cardiac insufficiency alone indicate digitalis. Increased heart rate alone is never the result of cardiac insufficiency and never the indication for digitalis therapy.

Paroxysmal tachycardia does not respond to digitalis and digitalis does not affect simple tachycardia. No murmur of whatsoever sort, nor enlargement of the heart, in itself is an indication for digitalis. Christian (Boston Med. and Surg. Jour., July 13, 1922).

Chronic myocarditis generally occurs in association with other more or less evident organic lesions, and in particular with arteriosclerosis. Where this condition is marked, digitalis should, of course, be used only with some circumspection. If the blood-pressure is not much raised, however, and there coexist pronounced symptoms of circulatory inefficiency, digitalis in small doses, it is now conceded by many, will often yield excellent results. In cases with marked emphysema and cyanosis, however, special care is required, as large doses of digitalis may cause sudden death. In these cases German clinicians prefer to use caffeine and theophylline sodium acetate (theocine).

In cases with high arterial tension digitalis is at first contraindicated; but in all these cases in course of time symptoms of heart-failure set in. In such cases at this period benefit may be obtained from the careful use of digitalis or strophanthus. It is often advisable to administer at the same time one of the vasodilators or the iodides. Formerly, the author employed the vasodilators alone or gave digitalis only in small doses, combined with full doses of the nitrites. He found, however, that in many cases he had no results unless he increased the amount of digitalis until full doses were reached and the blood-pressure had gained its former level; only then did edema disappear. In such patients digitalis is often demanded in fairly full doses to maintain blood-pressure at its high level, otherwise capillary circulation fails and venous stasis develops. A. D. Blackader (Therap. Gaz., Oct., 1908).

In cases of **arteriosclerosis** with vaso-motor control largely gone, the blood-pressure may be found, for instance, to be 280 mm. Hg in a case in which, the heart beginning to fail, there is some edema of the ankles and shortness of breath upon ordinary exertion. It might be thought that the best treatment would be to give drugs to diminish the blood-pressure. In practice, however, the best results are obtained by giving 15 minims (0.9 c.c.) of tincture of digitalis in water three or even four times a day. It might be thought that the patient would necessarily suffer from apoplexy, but in practice it is found that the risk of this does not seem to be any greater with the giving of the digitalis than without it. French (*Clinical Jour.*, July 5, 1911).

The writer found digitalis effective in many cases of circulatory failure. In 8 cases of **arteriosclerotic heart**, 6 were improved by digitalization. In 10 of **myocardial insufficiency** digitalized, 5 were benefited. In 6 cases of rheumatic heart, without failure, no benefit occurred. Four cases of rheumatic heart disease, mitral stenosis, regular rhythm, and congestive circulatory failure, were improved clinically by digitalization. In 1 case of **mitral stenosis**, digitalis produced depression of auricular conduction (prolonged P R interval) coincident with marked clinical improvement. Aortic regurgitation does not contraindicate the use of digitalis. In a case of complete block with congestive failure, digitalis produced clinical improvement. In this case the writer considers that the digitalis effect was probably a direct effect on the ventricular musculature. In 18 cases of relative high diastolic blood-pressure there was no evidence of effect from small doses of digitalis. Small doses of digitalis produced no constant or marked change in pulse pressure, systolic pressure and heart rate. There was no evidence that small doses of digitalis were of value in mitral stenosis, angina pectoris, hypertension and myocardial insufficiency. Leech (*Boston Med. and Surg. Jour.*, Feb. 26, 1925).

In the frequently met subjects of combined circulatory and renal involvement or "**cardiovascular-renal disease**," at a stage where, with the blood-pressure still high and the kidneys secreting urine of low specific gravity, the heart begins to fail and edema to appear, moderately large doses of digitalis will often bring considerable relief, the heart muscle itself being generally better preserved than in other myocarditides. According to A. Meyer, it is especially the cases with distinctly high blood-pressure that require fairly generous amounts of digitalis. Where the renal excretory function is already seriously compromised, however, full doses may bring on uremia by arresting the flow of urine. Hence it will not infrequently become a question whether digitalis should be used at all in these cases, small doses alone generally proving inefficient in overcoming the cardiac weakness.

Meyer suggests that where the vascular changes accompanying myocarditis are but slightly marked, 0.1 Gm. (1½ grains) of powdered digitalis be given thrice daily for a few days, then once or twice daily. Where they are more pronounced, or the patient's age is such as would lead one to suspect their presence, greater caution should be exercised, 0.2 to 0.3 Gm. (3 to 4½ grains) being given *per diem* for two or three days only, then 0.1 Gm. (1½ grains) for a day or two. Combination with a diuretic, at the beginning of treatment, may be advantageous.

**Valvular Disease.**—Consideration of the uses of digitalis in valvular disease may properly begin with **acute endocarditis**, since this is the natural precursor of deformity of the valves. The consensus of opinion is that digi-

talis should not be used in this condition until indications of actual heart weakening occur. Where the heart muscle is less impaired than the valves, as is usually the case, it seems clear that increasing the force of the heart beats with digitalis may be productive of more harm than good. The same applies to cases of **subacute endocarditis**, in which the inflammatory process in the endocardium and valves continues for weeks or months, with some febrile reaction and chills at irregular intervals. Rest in bed is the most important measure in the treatment of these cases.

In acute endocarditis especially, but also in acute myocarditis, the employment of digitalis is to be deprecated. In this condition absolute rest with low vascular tension is demanded; even regurgitation of the blood-stream is of value for the time being by lowering intraventricular pressure. All acute inflammatory symptoms must pass away completely before the administration of digitalis can be free from risk of harm. If stimulants to the general circulation at this time are demanded, strychnine, ammonia, camphor, and alcohol are to be preferred. A. D. Blackader (*Therap. Gaz.*, Oct., 1908).

As a rule in the **heart-failure of acute rheumatism** with failure of tonicity, while the infection is acute digitalis fails entirely, but at a later stage, when the temperature has been normal for some days, and dilatation increases with dropsy, its administration is sometimes of great value. H. Hume Turnbull (*Austral. Med. Jour.*, Oct. 19, 1912).

In **chronic endocarditis**, with gradually developing valvular fibrosis, or in cases in which defective valves remain as they were after subsidence of an acute or subacute inflammatory process, myocardial hypertrophy usually occurs to compensate for the mechanical disadvantage at which the

heart is placed owing to the valvular trouble. Where this compensation is sufficient to satisfy ordinary circulatory requirements, digitalis is rarely indicated. As soon as signs of cardiac insufficiency, such as dyspnea or cough on exertion, palpitation, slight edema, and indigestion appear, however, and most emphatically where the patient has already taken to bed when first seen, digitalis should be administered, and will often be productive of a remarkable degree of benefit. The indications for the drug vary somewhat in the case of lesions of the different valves, and the latter will therefore be taken up individually.

It is in **mitral insufficiency**, the commonest form of valvular involvement, that digitalis is most strikingly effectual and may be given with the least danger. As in every other cardiac disorder, the drug is especially valuable where dilatation of the cardiac walls can be detected by physical methods of examination, the tonifying property of digitalis rapidly drawing the insufficient ventricular walls together and increasing the functional efficiency of the organ. The prolonged diastole rests the muscle, the powerful systole improves the coronary circulation, and the increased tone may result in contraction of the mitral orifice and approximation of the papillary muscles and their tendinous prolongations to an extent sufficient to allow of better closure of the orifice during systole. The right ventricle, if overburdened, is relieved, congestion on the venous side of the circulation is overcome, and the functions of various organs are bettered through the removal of stasis.

If the writer's "digitalis test"—the giving of 25 drops of the French official



digitalin solution in every case of arterial or endocardial cardiopathy when compensation begins to fail—is negative, that is, if the heart does not show any tonic effect from it, other heart tonics are required,—strophanthus or sparteine. In case of transient trouble, with a resistant myocardium, the author gives large doses of digitalis followed by progressively smaller doses (constant effect). This is followed by a period of repose on a milk diet, returning to the digitalis in case of a new attack of heart weakness. In case of chronic trouble, with a degenerated or sclerotic myocardium, he commences with the digitalis test, and if the myocardium does not respond properly to the test he gives sparteine and strophanthus alternately for a week. When the heart has been steadied, he then gives the digitalis in a single large dose (25 to 50 drops in two doses), then follows with rest on a milk diet. Whenever the myocardium shows signs of wavering, then the heart tonics should be resumed first, and later the digitalin. The official digitalin to which he refers contains 1 mg. of active principle in 50 drops of the alcoholic solution. A case is cited to show how digitalis failed at first, but after the interposition of the heart tonics was able to exert its specific action and the patient was kept in comparatively good health by resumption of this alternate medication at need, with intervals of repose. Huchard (*Presse méd.*, No. 1, 1905).

The best results of digitalis are obtained in cases of **mitral disease** associated with a deficient heart muscle. These results are probably due to an improved coronary circulation resulting in better nutrition to the heart muscle. Digitalis, on the other hand, fails in those cases in which the irregular and rapid heart action is due to nervous influences. Notable examples of this are paroxysmal tachycardia and the rapid pulse of Graves's disease. Edens (*Therap. Monatsh.*, xxv. Nu. 1, 1911).

In **mitral or aortic valvular disorders** and in **myocarditis**, digitalis is useful where cardiac irritability is disturbed and the heart-rate somewhat accelerated.

Bordet and Yacoel (*Arch. des mal. du cœur*, Oct., 1924).

Not infrequently the physician will be called when the patient is in acute distress, sitting bolt upright or standing bent over and struggling for breath, with marked nervous excitement, accelerated and irregular pulse, cold perspiration, possibly coughing and precordial pain. Under these conditions digitalis, while indicated, will not act promptly enough; the immediate requirements are for a hypodermic injection of morphine, guarded, if respiratory depression is feared, by a small dose of atropine or a larger one of strychnine. An injection of nitroglycerin, repeated, if need be, until intracranial pulsation is felt subjectively, or venesection, will often relieve the dilated heart and cut short the symptoms, though in cases where there is marked collapse and prostration ergot intramuscularly may be preferable. Once the attack is subdued digitalis should be given, either in the form of the tincture, in doses of 10 to 20 minims (0.6 to 0.12 c.c.) two or three times daily, German digitalin,  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.0075 to 0.015 Gm.), or the infusion, 1 to 3 drams (4 to 12 c.c.). In the final stage of mitral insufficiency Abrahams administers, to begin with, even a 1-dram (4 c.c.) dose of the tincture, to be repeated in twelve hours if there has been no satisfactory symptomatic betterment; the dose is then reduced to 30 minims (2 c.c.) three times a day, this being continued for the next two or three days, and finally to 20 minims (1.2 c.c.). In the less advanced cases the same author gives 10-minim (0.6 c.c.) doses for an indefinite period. Absolute rest is to be enjoined when large doses are being

taken. It is also necessary to beware of toxic effects (see section on UN-TOWARD EFFECTS), the fact being kept in mind that the drug is slowly eliminated and a summation of the action of successive doses occurs, with a tendency to renal vasoconstriction and further accumulation. Occasional intermission for a few days is advisable. Where prolonged administration is necessary, Whitla interrupts the digitalis every two months, and after a three-day rest gives strophanthus in smaller doses, with syrup of iron, quinine, and strychnine phosphates. Most clinicians intermit more frequently, *e.g.*, every two or three weeks, a ten-day rest being given.

In 3 cases in which fluoroscopy showed cardiac dilatation during attacks of precordial discomfort and cardiac insufficiency, digitalis led to increased distention of the ventricle, whereas 10 to 12 intravenous injections of 0.25 mgm. ( $\frac{1}{200}$  grain) of ouabain brought relief. Bordet and Yacoel (Arch. des mal. du cœur, Oct., 1924).

It is often advisable, when beginning digitalis treatment, to prepare the ground for its action by preliminary catharsis and diuresis. The former effect may be secured, *e.g.*, by a full dose of compound jalap powder. A favorite procedure serving both cathartic and diuretic purposes is to combine the digitalis with squills and a mercurial, as in the so-called Guy, Addison, or Niemeyer pill:—

℞ *Pulveris digitalis*,  
*Pulveris scillæ*,  
*Massæ hydrargyri*. ãã gr. xxiv (1.5 Gm.).  
 Ft. pil. no. xxiv.  
 Sig.: One pill after each meal.

Calomel might be used in place of the blue mass, acting more strongly, though at times less pleasantly for the patient. Huchard substituted pow-

dered scammony for the mercurials, thereby relying solely on the squill for the direct diuretic effect, while Allbutt, in the presence of dropsy, combines the xanthin derivatives with digitalis:—

℞ *Theobrominæ sodio-salicylatis* (diuretin) ..... gr. x-xv (0.6-1 Gm.).  
 [vel *Theophyllinæ sodioacetatis* (theocin sodium acetate) ..... gr. iv (0.25 Gm.)].  
*Tincturæ digitalis*.. ℥v (0.3 c.c.).  
*Spiritus juniperi compositi* ..... ʒss (2 c.c.).  
*Aquæ carui* [vel *anis*] ..... ʒj (30 c.c.).

M. Sig.: For one dose.

Rest in bed and, in advanced cases, reduction of the intake of fluids are always to be remembered as powerful adjuvants to the favorable circulatory and renal effects of these drugs. Huchard limited the fluids in severe cases to 200 Gm. ( $\frac{7}{8}$  pint) of a mixture of 3 parts of milk with 1 of water, four times daily. On and after the fourth day whole milk was substituted, but the quantity kept the same until the third week, when 1500 to 1800 Gm. (3 to  $3\frac{1}{2}$  pints) were allowed. Solid food was given only when the patient ceased losing weight.

Patients with cardiac dilatation, whether the failure of the left heart is due to valvular diseases or to a primary myocarditis, should not be given digitalis when first seen. Instead the patient must be absolutely still in bed for at least twenty-four hours. Then digitalis can be given tentatively, in small amounts at first, gradually increasing the dose and feeling one's way with it until the proper degree of stimulation may be obtained. Some patients with primary myocarditis are distinctly harmed by digitalis. M. H. Fussell (Penna. Med. Jour., Nov., 1912).

The same author, and more recently Mayor, of Geneva, have advised the prophylactic administration of small doses of digitalis in heart cases, *i.e.*, the giving of the drug even during periods in which signs of insufficient cardiac function are but slight or absent. They consider it a mistake to leave off digitalis entirely when peripheral edema has disappeared. Huchard, in cases in which the myocardium is in the initial stages of degeneration, reduced the fluid intake for a short period every month or six weeks, and after this gave  $\frac{1}{650}$  grain (0.0001 Gm.) of the French "digitaline cristallisée" for ten days to two weeks. Attacks of heart weakness with peripheral edema can thus, according to this author, be put off or entirely prevented. Mayor, of Geneva, lays stress on the harm done to the various organs of the body, and hence to the system as a whole, by repeated attacks of heart weakness, and points out that if, after the first attack is passed, subsequent attacks are forestalled by periodic administration of small doses of digitalis, the general condition will be kept good much longer than would otherwise be the case and the ultimate serious circulatory breakdown materially retarded. The aim sought in giving small doses of digitalis, as advised by this author, is not to cause the heart to hypertrophy, but to maintain its ability to withstand temporary additional stresses, so that it will not at once become insufficient under the influence of emotional disturbances or when unusual muscular activity is indulged in. The condition to be established is the same as that seen in healthy individuals who take up mountain climbing in the spring, after

being inactive all through the winter; on the first day, dyspnea and tachycardia are marked and out of proportion with the work performed, but on the second they diminish and on the third are no longer noticed, circulatory sufficiency having been re-established in spite of the fact that during the short period elapsed cardiac hypertrophy cannot have occurred. The object is thus not to allow a heart bearing a permanent lesion to lose the habit of performing the maximal amount of work of which it is capable, in order that when unusual stress comes the organ will not be exposed to dilatation. Sometimes this result can be secured by means of carefully supervised muscular exercises or through hydrotherapy; but in many instances these measures are not at all or only partially available, and in these, according to Mayor's experience, digitalis is of great assistance. Usually 0.3 Gm. ( $4\frac{1}{2}$  grains) of digitalis, given in the course of three days three times in each month—on the 1st, 2d, and 3d, 11th, 12th, and 13th, and 21st, 22d, and 23d, of each month—is the amount required, though in some cases this may have to be increased to 0.45 Gm. (7 grains) or can be reduced to 0.2 Gm. (3 grains). The drug may be conveniently administered in the following form (Mayor):—

R *Fluidextracti digitalis*,

*Fluidextracti hydrastis* .....ãã 4 Gm. (℥lxxv).

*Glycerini* ..... 2 Gm. (℥xxx).—M.

Ten drops of this mixture, containing 4 drops (not minims) of the fluidextract of digitalis, are equivalent approximately to 0.1 Gm. ( $1\frac{1}{2}$  grains) of powdered digitalis leaf. When through some accidental circum-

stance the patient becomes unduly fatigued, or in the event of any acute infection, even slight—bronchitis or influenza, for example—occurring, the dosage of digitalis should be temporarily increased. By proceeding in this manner, Mayor asserts, circulatory sufficiency can be maintained for so long a time as to afford the patient an illusion of complete health.

After a more or less prolonged period, however, heart weakness will begin to appear in the intervals between periods of digitalis administration. The next step which suggests itself is to increase gradually the total amount of digitalis taken in each three-day period from 0.3 Gm. to 0.35, 0.4, and even 0.6 Gm. (5 to 9½ grains). This may be tried, but often better results are obtained by reducing gradually the intervals between the periods of medication to seven, then to six, five, and four days. Finally, a time will come when circulatory equilibrium will hardly be maintained by digitalis for more than twenty-four hours. The drug treatment will then have to be continuous instead of interrupted.

Groedel, Kussmaul, Sahli, and Henrijean have reported cases of cardiac disease kept free from further attacks of failure of compensation for six, seven, and even twelve years by the daily ingestion of suitable doses of digitalis. One of Groedel's cases, after repeated attacks necessitating long periods of rest and increasing doses of digitalis, was kept free from any further attacks and enabled to resume and continue his work as a surgeon for eleven years by 0.05 Gm. ( $\frac{1}{2}$  grain) of powdered digitalis leaves taken twice daily. In certain forms of **adhesive mediastinopericarditis** and

of **aortic insufficiency** in arteriosclerotics, in cases where an idiopathic hypertrophy gives way to fibrous myocarditis with rapidly recurring acute decompensation, and in a few cases where the right heart is constantly menaced by reason of a chronic lung affection and the patient for some reason cannot be kept under watch, Mayor advises that the digitalis treatment be continuous from the first, and not begun with the intermittent form.

In continuous treatment the question of cumulative action has to be considered. Pouchet and Mayor agree, however, that 0.0001 Gm. ( $\frac{1}{650}$  grain) of crystallized digitalin, *i.e.*, about 0.1 Gm. ( $\frac{1}{2}$  grains) of powdered digitalis leaves, does not exceed the amount that can be destroyed or eliminated daily by the adult human subject. If, with these small doses, signs of cumulative action should happen to appear (the patient being always instructed as to their nature) a single day's interruption would suffice, as a rule, to restore equilibrium. A second objection which might be raised to continuous treatment, *viz.*, that a premature and excessive compensatory hypertrophy would take place, is shown to be groundless not only by the fact recognized by various authors, including Sahli, that life can be prolonged by continuous administration of digitalis (because the effects of stasis in various organs, which react unfavorably on the heart itself, are thus avoided), but also by the experimental work of Cloetta (1908), which showed that *therapeutic* doses of digitalis do not cause hypertrophy of the normal rabbit's heart; in rabbits in which aortic insufficiency had been artificially es-

tablished, indeed, the drug was shown to render easier the work of the heart, for while among the animals not given digitalis the heart underwent hypertrophy to the extent of 80 per cent. and several succumbed to the cardiac disease, among those given therapeutic doses of digitalis the hypertrophy amounted only to 30 per cent. and none died until sacrificed for examination twelve to eighteen months after the production of the artificial lesion.

Report of cases showing the value of continuous administration of small doses of digitalis. One case was that of a woman 72 years of age, presenting dyspnea such that she was almost unable to walk, with cyanosis, marked stasis at the bases of the lungs, and murmurs at all the valves. Being placed upon digitalis, she took 620 powders each containing  $1\frac{1}{2}$  to  $2\frac{1}{4}$  grains (0.1 to 0.15 Gm.) of the leaves. She was then taken with pneumonia, but continued the powders, and recovered. At the time of writing, over four years after the beginning of treatment, she had taken in all nearly 1200 doses. During this period she tried several times to leave off the remedy, but after a few days felt impelled to resume it. On one occasion, however, three years after the beginning of treatment, she left off the drug, upon request, for a month, and on this occasion bore the interruption of treatment better than she had been able to before. The use of the drug was only resumed in order to avoid the bad effects of cold, which she withstood better when under the influence of the drug. The pulse rate was from 82 to 90, and seemed hardly to have changed at all since the heart action had been made regular for the first time at the beginning of treatment. Henrijean (*Bull. de l'Acad. roy. de Méd. de Belgique*, vol. xxii, Nos. 3 and 4, 1908).

In mitral stenosis opinions concerning the value of digitalis are not unanimous as in the case of insuffi-

ciency of the same valve. The drug sometimes fails to yield the benefit expected of it. There seems to be no question, however, that when the right ventricle weakens, digitalis may do much good by toning it up. The objection has been raised that the drug may do harm by increasing the pressure and congestion in the lungs, but, after all, this could probably only occur if the beats of the right ventricle became stronger than they had been before this ventricle weakened. It is also possible for digitalis to do good by slowing the cardiac rate, thus allowing more time for the left ventricle to become filled through the narrow mitral orifice. At any rate, the administration of the drug in moderate doses may be tried when symptoms of circulatory insufficiency appear, and, if it fails to benefit or is not well borne, it can later be withdrawn and caffeine sodiobenzoate in doses of 5 grains (0.3 Gm.) tried instead. In the more advanced cases of mitral stenosis, complicated with regurgitation at the same orifice, there is no question of the efficacy of digitalis, which may be given in full doses. Where the patient begins to complain of dyspnea, Fiessinger gives  $\frac{1}{650}$  grain (0.0001 Gm.) of the French "digitaline cristallisée" daily for ten days, then reduces the dose to  $\frac{1}{930}$  grain (0.00007 Gm.) for ten days, and alternates thus until the symptom is completely relieved; finally ten-day periods with  $\frac{1}{650}$  grain (0.0001 Gm.) are alternated, with like periods of complete intermission. The patient can thus very often be kept comfortable for a number of months.

In circulatory failure due to mitral stenosis, one should not only carefully weigh the import of the tumultuous

cardiac sounds, but by the use of instruments of precision determine, if possible, whether there is delay in the transmission of the contraction impulse over His's bundle. If such a delay exists, digitalis in doses large enough to cause a distinct and sharp cardiac effect is probably capable of prolonging this delay and so doing harm. If given at all, the dose of digitalis must be so small as to produce a very gradual effect, one which will not consist in decreasing auricular contraction through vagal stimulation, but gently re-establish general cardiac power. At first one should give the patient absolute rest, unload the portal system by free purgation, use venesection to relieve stasis, and give rapidly acting diffusible stimulants for a few hours until the co-ordination of cardiac movement is re-established. When this is done, small doses of digitalis, arsenic, and iron may be used. Hare (*Therap. Gaz.*, vol. xxvi, p. 244, 1910).

In cases of mitral stenosis with regular pulse, and those resulting from arterial disease, digitalis is often impotent or even harmful; the heart continues to dilate, and dropsy increases under its use. Windle (*Brit. Med. Jour.*, Feb. 25, 1911).

In cases of mitral stenosis, digitalis is contraindicated if the presystolic murmur is missing, the jugular or liver-pulse is synchronous with the cardiac systole, and the heart occasionally skips a beat, with a tracing showing disturbance in conductivity. Martinet (*Presse méd.*, July 8, 1911).

In **aortic insufficiency** it is, in general, the tonicity of the heart muscle that governs the administration of digitalis. Where, owing to insufficient coronary blood-supply, the muscle begins to dilate and the cardiac dullness shows enlargement greater than that corresponding to the primary excentric hypertrophy of the organ occasioned by the aortic leakage, the drug is in many instances capable of considerable benefit provided the dose

is carefully adjusted. A seeming danger in these cases is that the cardiac rate may be unduly slowed by the drug, with resulting excessive prolongation of diastole, and hence—in this form of valvular disease—of the periods of blood stagnation in the vessels, the nerve-centers being meanwhile exposed to the evil effects of repeated temporary anemia. But by giving only small doses of digitalis the tonifying effect of the drug on the heart muscle can be obtained with relatively little change in the rate; upon cautious use digitalis can thus be made to do good where larger doses would do harm. Abrahams, for example, gives 5 minims (0.3 c.c.) of the tincture three times on the first day, 6 minims (0.35 c.c.) three times the second day, and continues to increase gradually until the desired effect is produced or the maximal dose of 20 minims (1.25 c.c.) three times a day is reached, when the initial dose is resumed and kept up indefinitely (preferably with an intermission of eight or ten days in each month). The patient should always be required to stay recumbent and be kept under rather close watch, so that the drug can be at once interrupted or the dose reduced if untoward symptoms should appear. It is recommended not to allow the pulse rate in these patients to fall below 80, in order to avoid anemia of the centers. The efficiency of atropine in abolishing vagal action where this is causing undue slowing of the heart rate is to be borne in mind. This drug may not only be used to exclude the vagi where syncopeal phenomena appear, but given prophylactically with the digitalis to prevent too great a diminution of rate. In advanced cases of aortic re-

gurgitation relative insufficiency of the mitral valve is likely to appear, the heart muscle having yielded to such a degree that the mitral leaflets can no longer come in contact across the orifice. Under these conditions digitalis is clearly indicated, though some caution in the dosage remains necessary, lest sudden cardiac failure should take place.

The danger of giving digitalis in **aortic regurgitation** is entirely illusory. Sometimes, as in certain aortic lesions or in arteriocalillary sclerosis, it may be well to combine it with nitroglycerin or some other vasodilator, but even this precaution is usually unnecessary. A. E. Taussig (*Interstate Med. Jour.*, Aug., 1912).

The old objection to digitalis in **aortic regurgitation** on the ground that prolongation of the diastole would allow an increased quantity of blood to pass back into the ventricle, is still held by some, but in the vast majority of cases it will be found that no slowing of the pulse is produced by the drug, while its action on the cardiac muscle may prove of great value. H. Hume Turnbull (*Austral. Med. Jour.*, Oct. 19, 1912).

As soon as **aortic regurgitation** is accompanied by failing heart action, as shown by swelling about the ankles, pulmonary congestion, and other well-known signs, digitalis is the drug to be used. The same thing applies to **Adams-Stokes' disease**: When dropsy occurs, with enlargement of the liver, digitalis is indicated even if marked bradycardia is present. David Riesman (*Penna. Med. Jour.*, Nov., 1912).

True, uncomplicated **aortic stenosis** is infrequent. Much oftener the condition is merely a roughening occurring in conjunction with more or less widespread angiosclerotic changes, and not infrequently combined with aortic leakage. In all forms compensation is likely to be maintained for a

prolonged period, and no heart tonic will therefore be required. When the muscle finally gives way to dilatation, considerable myocardial fibrosis or degeneration will usually have occurred, particularly in aged patients, and moderation in the dosage of digitalis will consequently be indicated. Where, again, stenosis exists without pronounced myocardial disease, some authors contend that the free use of digitalis involves danger of vascular rupture, owing to the fact that the heart is greatly hypertrophied and will be aroused to powerful activity by the drug. On the whole, the point to be chiefly observed in using digitalis in aortic stenosis is thus moderation in dosage, except in the last stages. Relief of precordial discomfort will afford an indication as to whether the drug is proving of assistance to the heart or, on the contrary, is inciting it to excessive activity. Where the discomfort is increased, strychnine or caffeine may be substituted. In the earlier stages of aortic stenosis it may sometimes happen that the phenomena accompanying palpitation—the latter induced by some temporary emotional disturbance—are mistaken for heart-failure, and digitalis given; under these conditions the symptoms may be aggravated owing to the more or less marked muscular hypertrophy, and cardiac sedatives will be indicated instead.

In **tricuspid regurgitation**, a condition seldom uncombined and usually occurring as evidence of an overworked right ventricle owing to the presence of mitral leakage or obstruction in the pulmonary circulation, digitalis is generally not of the same striking degree of utility as in mitral insufficiency. While in the less severe

uncomplicated cases it is capable of giving excellent results, a large proportion of patients with tricuspid insufficiency come under observation when cardiac enfeeblement is already far advanced, and the organ may fail to respond to digitalis as one might expect. In these refractory cases Fränkel recommends the intravenous administration of strophanthin. If it is not desired to resort to this extreme measure, digitalis in moderate doses, preferably in combination with theobromine or caffeine (A. Meyer), may be employed.

In 17 **mitral insufficiencies** with more or less compensation 15 reacted promptly and 2 with defective compensation negatively. In 4 cases of pure **mitral stenosis** 2 did not react; 1 was a case of hepatic stagnation, the other of dilatation and pulmonary infarction. In 31 with combined mitral insufficiency and mitral stenosis all reacted but 2, and in 1 of these there was severe myocarditis. Of 9 cases of **aortic insufficiency** digitalis was negative in 2, in 1 of which there was dilatation. When negative results could not be associated with cardiac conditions they could be traced to severe general or pulmonary affections. In several cases of association of tricuspid and mitral lesions the result was not significant, as there was as a rule dilatation of the right heart and stagnation of the liver. In 30 cases of associated aortic and mitral lesions the behavior under digitalis was very irregular, and there were at least 9 negative results in which various complications were accused. Of 33 affections of the myocardium, chiefly **chronic myocarditis**, there were 5 negative results which included 2 cases of goiter heart. In 5 cases of pericarditis with exudation, in which hepatic stasis coexisted, there was no reaction of any value. In nearly all the 21 cases of **cardiac insufficiency of chronic nephritis** (no manifest arteriosclerosis) the reactions were marked. In 13 cases with **arteriosclerosis** the results were

good in 7. Here as elsewhere the increase of diuresis was one of the evidences of a positive reaction. Total failure generally argued a poor state of the cardiac muscle. Schrenk (*Med. Record*, from *Münch. med. Woch.*, Dec. 31, 1912).

In **tricuspid stenosis** and in **pulmonary insufficiency** or **stenosis**, all infrequent lesions and usually congenital, the same considerations apply as in corresponding disorders of the left side of the heart, dilatation and weakening of the ventricular muscle constituting the chief indication for digitalis.

**Cardiac Irregularity.**—Relatively recent clinical studies, conducted with the aid of improved instruments such as the polygraph, have shown that the various forms of cardiac arrhythmia are reducible, according to their mode of production, to six fundamental types, viz., sinus arrhythmia, heart block, premature contractions, paroxysmal tachycardia, auricular fibrillation, and alternation of the pulse. Since these different forms present more or less definite and diverse indications in regard to digitalis therapy, it will be advantageous to discuss them individually. The subject as a whole, however, is one that cannot be divorced from organic heart lesions, and it is from considerations of simplicity and clearness alone that no mention was made of the arrhythmias in the preceding sections. Since each of the forms of irregularity can occur in association with a number of different organic or functional cardiac disturbances, it will be essential to state in every instance, as precisely as is now possible, the field covered by the arrhythmia under consideration.



**Auricular fibrillation**, according to Lewis the commonest of the arrhythmias, was formerly termed nodal rhythm by Mackenzie and represents one variety of what is frequently called the "permanently irregular pulse." The rhythmic stimulus which sets the heart in motion at each beat, normally developed at and propagated from the region of the sinus, *i.e.*, at the junction of the superior vena cava with the right auricle, is superseded in auricular fibrillation by the formation of abnormally frequent, irregular stimuli in the auricle, which not only result in loss of co-ordinate contraction in this chamber itself, but are transmitted in their haphazard succession to the ventricle. The latter, in turn, responds in so far as it can to the impulses received and contracts both at irregular intervals and with varying amplitude of beat. The rate is, as a rule, increased to 110 to 150. About one-half of all cases of this form of irregularity occur in mitral stenosis, almost one-fourth in myocardial degeneration, and the remainder in aortic disease, arterial disease and granular kidney. In nearly all hearts beating irregularly at a rate exceeding 120 the arrhythmia represents auricular fibrillation (Lewis). Constant irregularity, without intervening periods of regular rhythm, is characteristic. The symptoms are those of a failing heart muscle, sometimes with subjective sensations of precordial fluttering. In the less advanced cases of heart disease, however, attacks of fibrillation may occur at long intervals without giving rise to much disturbance. In general, auricular fibrillation is of unfavorable prognostic significance, few cases living longer than ten years after it

has set in. The higher the heart rate the more serious the condition. It is in this type of irregularity, however, that digitalis is of greatest value. By impeding the transmission of the weaker impulses from the auricle to the ventricles, through diminished cardiac conductivity, the drug shields the ventricles from overwork by reducing their rate of contraction, and frequently produces a most striking improvement in the patient's condition. In the average case the tincture should be given in doses of 10 or 15 minims (0.6 to 1 c.c.) three or four times a day, the patient being meanwhile kept in bed. If a drop in the pulse rate should fail to occur in a few days, the dose may be increased until signs of intoxication occur. In most instances, however, the rate will promptly fall, and when it reaches 60 to 80 the drug can be stopped, later to be resumed in doses of 5 minims (0.3 c.c.) if acceleration tends to recur when the patient rises from bed. In the most serious cases, with a rate of 170 to 200, strophanthin intravenously in the dose of  $\frac{1}{250}$  grain (0.00025 Gm.), repeated once or twice at bi-hourly intervals, may be substituted for large doses of digitalis (Lewis).

The total amount of tincture of digitalis required in **auricular fibrillation** to produce runs of coupled beats or regular slowing is, on the average, 450 minims (30 c.c.)—that is, in about ten days with doses of 15 minims (1 c.c.). Digitalis should be stopped when this occurs. Within two or three days the pulse quickens and is again characteristically irregular. The drug should now be given again in increasing doses of from 10 to 15 minims (0.6 to 1 c.c.) three times a day, until the pulse slows to a rate approximating that at which the double beats previously occurred; it is with this rate of pulse that the patient will generally be at his best.

Windle (Brit. Med. Jour., Feb. 25, 1911).

In the absence of instrumental aid, the following plan should be adopted in cases of **auricular fibrillation** in which extrasystoles are present and vitiating the true reading of the effect of digitalis. First count over the apex with a stethoscope the total beats during the space of a minute; then count for another minute the number of coupled beats heard. Finally subtract the number of these coupled beats from the total beats; the result indicates the degree of ventricular response to auricular stimuli, and consequently the degree of blocking effect of the drug employed. A much truer indication of the effect of the drug can thus be obtained, and a safer control effected. Lea (Med. Chronicle, May, 1912).

In **auricular fibrillation**, digitalis acts by impairing the conductivity of the bundle of His. If it is given in sufficiently large doses—and very large doses are required—the bundle becomes less and less able to transmit impulses from auricles to ventricles, and the latter, instead of responding to each considerable tremor of the former, contract only after the strongest ones. The result is a very marked slowing of the ventricular rate of contraction, much greater than in other cases of broken compensation, with all of the accompanying benefits to myocardium and circulation. If the digitalis be pushed unduly, a complete block of the bundle of His may result. The heart then beats very slowly, 30 to 40 times per minute and entirely regularly, with the exception, perhaps, of an occasional extrasystole. This complete heart block is usually only temporary, ceasing as soon as the digitalis is discontinued. A. E. Taussig (Interstate Med. Jour., Aug., 1912).

The most striking results of digitalis are seen in cases where the rhythm of the heart is given by the fibrillating auricle. But when **auricular fibrillation** is not accompanied by a rapid pulse, there is no very marked effect; improvement occurs but slowly. When, however, there is a very rapid irregular pulse, digitalis is followed by a rapid

fall in the pulse rate and an improvement in all the symptoms. The slowing of the pulse may be used as a gauge of the action of the drug, and also as an indication as to whether the treatment should be continued. The slowing is not inhibitory in origin, for it remains after large doses of atropine. The auricle continues to fibrillate as before, and the digitalis may therefore be presumed to act either in the bundle of His or in the ventricle itself. Careful percussion in the author's cases failed to show any change in the limits of cardiac dullness in many cases in which obvious improvement in the symptoms occurred under treatment.

A dram (4 c.c.) of the tincture a day was first prescribed. This very often led to headache, nausea, or vomiting after a few days, or the pulse showed distinct effects; the drug was next abandoned for a few days, and then resumed with rather smaller doses. In many cases the best results were obtained at first only when the largest doses were taken which did not induce gastric symptoms. After a course of digitalis lasting for a fortnight or more, the patient often relapsed on giving up the drug. Renewed treatment restored the improvement, and finally a satisfactory condition could be maintained with comparatively small quantities or with larger amounts taken at intervals of several days. Since distinct improvement is rarely seen before the fourth day of treatment with digitalis, this precludes its use in the most acute cases. To elicit a more rapid effect the author injected strophanthin intravenously ( $\frac{1}{250}$  to  $\frac{1}{100}$  grain—0.00026 to 0.00065 Gm.) in a number of cases with most satisfactory results. Gibson (Brit. Med. Jour., Sept. 21, 1912).

Occasionally cases of **auricular fibrillation** are seen where the patient is not comfortable unless the dose of digitalis taken is large enough to maintain the coupled beats. In such cases the heart muscle is probably very badly affected, and no definite rule as to dose can be laid down. The physician must decide each case on its merits. It is important to remember that these small extra

beats may not be palpable in the radial pulse, so that the physician may be deceived on feeling this, but they are easily recognized on auscultation. H. Hume Turnbull (*Austral. Med. Jour.*, Oct. 19, 1912).

In **auricular fibrillation**, it is in the younger persons of the rheumatic group, especially if they have initial rapid pulse rate, that digitalis acts most successfully. In the non-rheumatic group (in which the persons are usually older) the results are not so encouraging. By the "atropine reaction" it is frequently demonstrated, especially in certain non-rheumatic fibrillating cases, that the slowing under digitalis is entirely vagal. The degeneration in the heart muscle in these cases seems to have reached a degree which renders it no longer capable of improvement. On the other hand, in the rheumatic group the atropine test proves the slowing is due to both vagal stimulation and cardiac tissue improvement. The latter being often much the larger factor, this shows that these hearts have a muscle capable of being helped.

When there is fibrillation, a patient with a pulse exceeding 100 while at rest needs digitalis. He should have 15 minims (1 c.c.) of the tincture or 1 to 2 drams (4 to 8 c.c.) of the infusion three or four times a day regularly, until the pulse slows to 70 or the physiological limit for digitalis is reached, as shown by headache, nausea, vertigo and possibly diarrhea. Not infrequently the first marked fall in pulse rate does not come until this physiological limit is reached. The drug should then be stopped. In some patients the pulse rate does not accelerate after the withdrawal of the drug, and there is little increase as the patients get up and around, until some new strain provokes a new attack. In a second group the pulse rate tends to accelerate after the digitalis is withdrawn, especially when the patients get up, but it can often be held in check by small doses, 5 minims (0.3 c.c.) two or three times daily. In a third group the larger doses of digitalis are necessary continually to keep the pulse rate in reasonable bounds.

These are probably the patients where the entire slowing is due to vagal inhibition. J. A. Talley (*Penna. Med. Jour.*, Nov., 1912).

In heart failure due to **auricular fibrillation** and a high grade of pulse deficit, the writers found that complete recovery from the attack not infrequently follows the beginning restoration of the circulation by a relatively small dose. In other similar cases this does not occur, and it is necessary to push digitalis. Eggleston and Wyckoff (*Arch. of Int. Med.*, Aug., 1922).

Of 150 cases of heart failure clinically studied by the writer, 6 per cent. had **auricular fibrillation**, while 94 per cent. had normal rhythm starting at the sino-auricular node. The smallest dose of digitalis required to induce toxic effects was 9 drams, the highest was 29 drams, and the average was well over 14 drams. This result is partly due to loss of potency of the tincture and partly to increased decomposition in the alimentary tract and liver. Bose (*Indian Med. Gaz.*, Apr., 1925).

**Premature contraction** (extrasystole) refers to a condition of arrhythmia in which, with the heart beating normally a part of the time, there arise now and then, either in the auricles or ventricles, impulses peculiar in that they come too soon, a single premature beat of the heart thus taking place which is usually weaker than the normal beats owing to the fact that not enough time has elapsed since the preceding contraction for the heart to be thoroughly prepared for the next. The extra beat may or may not be felt at the wrist; in the latter event a long interval is noted between successive pulsations to which the term "intermittence" is commonly applied. Premature contractions occur in association with a large variety of disturbances, both cardiac and extracardiac, and of very diverse severity; they possess, there-

fore, but little direct prognostic significance. Among the organic cardiac disorders, they most frequently accompany myocardial degeneration, next aortic disease and mitral stenosis, and finally, in occasional instances, angina pectoris, Bright's disease, and arteriosclerosis. Associated in other cases are gastrointestinal disturbances with gaseous distention and indicanuria, pulmonary tuberculosis, toxic influences such as may depend upon the excessive use of tobacco or the caffeine beverages, or free administration of digitalis itself, and numerous other conditions. Extrasystoles are an evidence of excessive irritability of the heart, and frequently occur in individuals with neurotic tendencies.

In most cases the administration of digitalis is neither desirable nor useful, sedatives such as the bromides, with measures directed to the removal of the cause, being indicated.

In primary **chronic myocarditis**, so-called, digitalis should not be used if there are extrasystoles, unless the heart has become incompetent, as shown by tachycardia, dilatation, dyspnea and the signs of passive congestion. The best results in broken compensation are obtained if digitalis is given in massive doses. A dram (4 c.c.) of the tincture daily is a moderate amount (divided doses). In about two days the maximum therapeutic effect will usually have been produced. The dose may then be cut in half. A. E. Taussig (*Interstate Med. Jour.*, Aug., 1912).

Digitalis is indicated when any symptoms are present which can be accounted for by no other cause than **myocardial insufficiency**. Benefit may follow large oral doses in **chronic myocarditis** with signs of cardiac failure. Repeated clinical observations have disproved the view that **pulsus alternans** contraindicates digitalis. Anderson (*Annals of Clin. Med.*, Sept., 1924).

**Sinus arrhythmia** (pneumogastric arrhythmia, Satterthwaite) is a comparatively infrequent type of irregularity characterized by a periodic waxing and waning in the rate and amplitude of the heart beats, and is dependent upon the influence of overactive vagi, which at corresponding intervals cause changes in the activity of the sinoauricular node, or pacemaker of the heart. The disturbance is generally of no significance, and requires no special treatment. Digitalis in full doses may itself produce it.

**Heart block** is characterized in general by an abnormally low cardiac rate (bradycardia) and is an expression of diminished conducting power in the auriculoventricular bundle, a slender neuromuscular band of tissue through which the contractile impulse is conducted from the auricle to the ventricle. Heart block may be either partial, in which case a certain proportion of the ventricular beats fail to occur, but relationship of the others to the auricular beats is still preserved, or complete, when both the auricle and ventricle beat regularly but at entirely independent rates, that of the ventricle slower than in the case of the auricle. Dropped beats in heart block differ from extrasystoles in being completely lost to precordial auscultation, whereas most extrasystoles can be detected as feeble ventricular beats by this method; the jugular pulsations will, besides, be found, on inspection, more frequent than those palpable at the wrist. Many cases of heart block occur among the elderly, and the condition is usually an indication of more or less widespread cardiac or cardiovascular changes, especially those such as result from syphilis and rheumatism.

It may also be due to irritation of the vagus or vagi through compression by neoplasms at any part of their course, occur temporarily in various acute infections, and be induced by digitalis and allied drugs. In most instances vagal influences, including that excited by digitalis, only bring on heart block where the conducting power of the bundle of His is already impaired, but occasionally the condition can be induced without any previous disturbance (Josué and Godlewski). In any case, it is clear that digitalis is contraindicated in the presence of heart block, except if there be pronounced cardiac dilatation, when the drug may prove useful notwithstanding a further slowing in the rate; or where complete heart block already exists, when the rate of the ventricular beats may be actually increased by the drug. Care in dosage is, however, necessary, at least in the former variety of cases, as observations of Taussig have shown that by pushing digitalis where there is partial heart block, injury may be done to the already weakened bundle, a permanent complete block resulting and the patient's condition becoming worse.

Case of a man aged 48, who had steadily grown more dyspneic, and was confined to bed. Physical examination showed a dilated heart, a mitral leak, evidence of atheroma of the aortic valves, pulmonary edema, an engorged liver and great anasarca of the legs. The radial pulse was 82 per minute, every fourth or fifth beat dropping out. The sphygmogram showed a condition of partial heart block. The myocardial incompetence was so marked that digitalis seemed indicated in spite of the evidence of impaired conductivity; mistakenly, as soon appeared. He was given 15 minims (0.9 c.c.) of the tinc-

ture three times daily. On the third day, the pulse, which had been 80, dropped to 60, and then lower and lower until, in spite of the discontinuance of the digitalis, it reached 32 beats per minute. The diagram of the pulse rate shows that the digitalis effect was not produced until after the drug had been given forty-eight hours, but persisted for a week or more after its discontinuance. The sphygmogram usually showed complete dissociation of auricular and ventricular contractions, though occasionally every second auricular beat went through. The patient's condition meanwhile had grown subjectively much worse. Finally, he had a brief attack of faintness, suggesting a Stokes-Adams attack. He was taken off digitalis and put on theocin 5 grains (0.3 Gm.) *t. i. d.* A great polyuria set in, he grew rapidly better, the heart block again became partial, as shown by the sphygmogram, and the pulse rate rose to between 65 and 80.

It has been shown by Erlanger and Hirschfelder that heart block which is complete when the auricles are beating rapidly becomes less so if the auricles are slowed. If in such a case one gives large doses of digitalis, the auricles beat more slowly, the block becomes less complete, and the ventricles may beat more rapidly, if somewhat irregularly. A. E. Taussig (*Interstate Med. Jour.*, Aug., 1912).

**Paroxysmal tachycardia** corresponds to the condition usually known as "cardiac palpitation," and consists essentially of a regular series of premature beats, all started at a single point in the heart, which point is generally other than the sinoauricular node, whence the contractile impulses normally arise (Lewis). The heart rate usually rises considerably above 100 per minute, and a characteristic feature is that the disturbance of rhythm occurs in attacks or paroxysms, which are of variable duration. The condition can probably not be said definitely to indicate cardiac disease, for

in most instances no sign of a valvular lesion can be found. In some patients, however, a tendency to dilatation of the heart and dyspnea on exertion is noted. The valvular lesion most frequently accompanied by paroxysmal tachycardia is mitral stenosis. Emotional stresses or exertion, acute illness, overeating; indulgence in coffee, tea, or alcohol; digestive disturbances, and the assumption of certain positions, are the commonest determining causes of paroxysms. In some cases, however, no exciting factor can be found in association with the attacks. For their relief, digitalis is only occasionally of service, and it is not possible to tell in which cases it will prove useful. A single full dose may arrest the paroxysm, but frequently the assumption of a certain posture—known to the patient alone—an ice-bag over the precordium, emesis or the relief of flatulence, and the administration of bromides or morphine, are more effectual. Vaquez advises that where, in spite of appropriate measures, a paroxysm continues more than three or four days and signs of serious heart weakness appear,  $\frac{1}{130}$  grain (0.0005 Gm.) of amorphous strophanthin be injected intramuscularly; on the next day, if necessary,  $\frac{1}{65}$  grain (0.001 Gm.) by the same route, and on the third day, if required, the last-named dose intravenously. In treatment during the intervals, the utility of digitalis seems largely limited to cases where evident cardiac disease is present, though Lewis states, without referring in particular to these cases, that a full course of digitalis (at first pushed until symptoms appear) may ultimately bring about improvement, and Carnot and Baufle have reported a

case in which continuous administration of small doses gave good results.

In 2 cases of **tachycardia** under the observation of the writer, the beats arising from an abnormal point in the heart, digitalis caused return to a normal rhythm, first inducing fibrillation of the auricle. Mackenzie (*Heart*, vol. ii, 273, 1911).

To be distinguished from the relatively infrequent cases of true paroxysmal tachycardia are numerous instances also commonly labelled "palpitations" in which an excessive heart rate is more continually present, as in the "irritable heart" of neurotic patients, athletes, or soldiers; tobacco, coffee, tea, or alcohol addicts, and mentally overworked individuals. Here the subjective sensation of a strongly beating heart is usually more pronounced than in paroxysmal tachycardia, but simple measures are more likely to bring relief where there is distress and the removal of the cause is usually more or less easily accomplished. Digitalis is generally inappropriate and unnecessary, unless the heart is weak. The same is true in the case of tachycardia induced by excessive thyroid activity, as in exophthalmic goiter, and in infections such as tuberculosis. On the other hand, in the "palpitation" experienced where the heart is acutely dilated owing to overexertion, digitalis is highly efficient.

**Alternation of the pulse**, the sixth and last distinct form of arrhythmia, consists in a succession of beats regular as to time, but in which alternate beats show a constant difference in size. It occurs (1) as an accompaniment of paroxysmal tachycardia, when it is of but slight importance; (2) in cases of angina pectoris, high arterial pressure, renal disease and fibrous

myocarditis (Lewis), when it is of distinctly unfavorable prognostic significance, signifying that the heart is overburdened and cannot long hold out, and (3) occasionally as a sign of digitalis intoxication. The alternation is generally but slightly marked and detectable only by sphygmography, though even under these circumstances it loses none of its evil portent when associated with organic cardiovascular-renal disease. The chief desideratum in these cases is less work for the heart, and hence, primarily, physical quiet and removal of factors tending toward mental excitement. The indications for digitalis vary and cannot be definitely stated. While a number of authors have observed the appearance or accentuation of pulsus alternans upon administration of digitalis, Wenckebach has seen the drug remove this form of irregularity in several patients, to the extent that even active exercise failed to cause it to return.

In true **angina pectoris**, associated with coronary disease or aortitis, digitalis is contraindicated. In angina accompanying myocarditis, however, Fiessinger asserts that digitalis in very small doses in conjunction with theobromine (considered a coronary vasodilator) may sometimes do good, though rest in bed is, in general, the best measure of all for relieving the pain. Where the condition is encountered in interstitial nephritis, the same combination (digitalis in small amounts only), together with the dietetic and eliminatory measures appropriate in this affection, will nearly constantly bring about improvement. Meyer points out the fact that in the presence of mild degrees of cardiac insufficiency the result of myocar-

ditis, mere extrasystoles and slight hepatic stasis may be the cause of angina. Under these circumstances small doses of digitalis may prove promptly effectual. In angina pectoris without evidence of insufficiency, on the other hand, digitalis may do positive harm; diuretin (theobromine sodium salicylate) in full doses should be administered instead. In the so-called "pseudoanginas," in which pain is referred to the heart in the presence of digestive disturbances, gall-stones, left-sided dry pleurisy, intercostal neuralgia, etc., digitalis is, of course, contraindicated unless evidences of poor circulation coexist, when small doses of the drug may prove useful.

In **acute pericarditis** digitalis is not of value unless there are indications of a tendency to heart-failure. When it is given, close observation of its effects is necessary, lest the increased amplitude of beat occasioned by digitalis be unduly hampered by the pericardial effusion, and the drug, owing to the slowed heart rate, therefore diminish instead of increasing the output of the heart. Where the right ventricle becomes dilated in pericarditis, Brunton considers diuretin more useful than digitalis. In **chronic adhesive pericarditis**, the drug is occasionally productive of good results in cases where marked myocardial changes do not as yet exist. When progressive cardiac insufficiency is encountered, however, digitalis is less effective than where the phenomena of stasis arise from causes other than adhesive pericarditis (Kovács).

**As Circulatory Stimulant in Emergencies.**—Although digitalis is especially suited for use in chronic disorders of the heart, its powerful exciting and tonifying effect on the

myocardium and stimulant action on the vasomotor center also render it valuable for the treatment of acute circulatory depression, as in **collapse** under anesthesia, **shock** due to a variety of causes, severe **ptomaine poisoning**, **mushroom poisoning**, and poisoning by circulatory depressants such as **aconite**, or, in fact, by any drug which in the later stages of its effects brings about the same condition, *e.g.*, **acetanilide**, **alcohol**, **chloral hydrate**, etc. In all these conditions the relative slowness of action of digitalis should be remembered, more quickly acting agents, such as ammonium compounds, ether, caffeine or coffee, strychnine, atropine, adrenalin, and the saline infusions being administered at the same time as the digitalis in order to sustain the circulatory functions until the foxglove begins to take effect. The methods of giving digitalis in these cases have already been referred to. (See **MODES OF ADMINISTRATION.**)

**Miscellaneous Other Conditions.**—Digitalis has been recommended in a number of affections not essentially circulatory in nature. Its effects in most of them are of a far less certain and striking character than in the disorders already discussed, and are not explainable on the basis of our present knowledge of digitalis pharmacodynamics, except in so far as the action on the circulation may participate in any benefit produced.

Stress laid on the continuous administration of digitalin in the nutritional disturbances of senility. The author has seen otherwise failing treatment converted into success by the addition of digitalis in cases of **ununited fracture**, **ulcers**, **edema**, **effusions**, and the **albuminuria** due to passive hyperemia. **Senile vesical paralysis**, with its neces-

sary accompaniment, catheterization, may be overcome by prolonged use of digitalis. Beates (Monthly Cyclo. and Med. Bull., Sept., 1912).

Digitalis is very useful in **hypertension** or **interstitial nephritis** sufficiently advanced to produce irregular pulse, lowered blood-pressure and edema. H. Vaquez (Arch. des mal. du cœur, Oct., 1924).

Thus in **pneumonia**, both **lobar** and **lobular**, a number of authors have maintained that digitalis exerts a favorable effect, the mortality, indeed, being reduced according to Petresco, Fickl, and Bloch. Frequently repeated doses of a strong infusion were formerly advocated by adherents of the "specific" digitalis method. Barth gave as much as 45 grains (3 Gm.) of the powdered leaves a day, exhibiting it every two hours in an infusion with rum and syrup of orange-peel. Slight vomiting and vertigo were not considered contraindications, though an abnormally slow or an irregular pulse were taken to indicate discontinuance of the remedy. Although it exerts no special beneficial effect on the disease process, it is useful to brace the heart.

Fever, it has been claimed, diminishes the efficiency of digitalis; this drawback may sometimes be overcome by the simultaneous application of an ice-bag over the heart.

In **pneumonia** the heart often responds beautifully to digitalis, and indeed it may be well to give it, in moderate doses, from the beginning of the illness. Here the heart-failure may be due not so much to the toxemia as to the obstruction to the lesser circulation induced by the massive consolidation of the lungs. There is thus a relatively unimpaired heart, struggling under an unusual load, and one may rationally expect it to respond to stimulation. When the heart-failure is due to toxemia, digitalis is quite as ineffective in pneumonia as in other infections.



A. E. Taussig (Interstate Med. Jour., Aug., 1912).

The Eggleston method is a valuable addition in digitalis therapy. It gives confidence in the use of the drug, and the shorter time necessary for securing digitalis effects should give the method wide use. The method must be used with care to select cases in which these effects are desired. In cases of decompensation with auricular fibrillation, it gives strikingly favorable results, but, with 3 or 4 c.c. (48 minims or 1 dram) or more of the tincture given daily for, several days, has resulted, once in partial and once in complete heart block. White and Morris (Arch. of Internal Med., June, 1918).

In various other infections, *c.g.*, **typhoid fever, diphtheria, septicemia and pyemia, plague, etc.**, similar considerations apply. The drug should not be used empirically, but for the specific purpose of overcoming circulatory weakness. Due caution should be exercised in the initial dosage, for if there is acute myocardial degeneration large amounts may prove harmful.

In the acute infections, the action of digitalis on the heart muscle is counteracted by the pyrexia, by the depressing action of the toxins upon the heart muscle, and by the often associated vasomotor paresis affecting chiefly the vessels in the splanchnic area. But in many cases it can be employed with advantage, although the results obtained are often not very manifest. Caffeine and camphor appear to have a more definite action. A. D. Blackader (Therap. Gaz., Oct., 1908).

Upon the heart seriously impaired by **typhoid** infection digitalis exerts a favorable and frequently a directly life-saving influence. In severe cases a combination of digitalis with small doses of ether, as recommended by von Jaksch, is indicated for the purpose of securing a more rapid action. Skutetzky (Med. Klinik, No. 22, 1911).

Other conditions in which the use of digitalis has been advised, seemingly with less justification, include **hydrocephalus, epilepsy, the insanities, hemoptysis, bronchial asthma, and spermatorrhea**. It has also been considered helpful in the reduction of **incarcerated hernia** and for the prevention of **abscess** formation.

Digitalis used to arrest the tendency to spontaneous **epistaxis** in 84 cases. In 75 per cent. of the patients the tendency to nose-bleed was promptly and permanently arrested within twenty-four hours after taking the digitalis, even in a few cases in which the bleeding was due to some anatomical abnormality, correction of which later permanently arrested the tendency. Focke (Therap. d. Gegenw., Sept., 1910).

Hemorrhage from the lungs is not due to tuberculosis in as large a proportion of cases as is generally assumed. Among the most important other causes are **anemia, arteriosclerosis, bronchial asthma, and acute catarrhal bronchitis**. In these conditions the **hemorrhage** occurs almost invariably from local congestion, inducing diapedesis. As the diapedesis occurs only from local stasis, treatment should aim to regulate the circulation in the region, and for this nothing is so effectual as digitalis. The proper measures are diet, keeping the bowels open and regulating the circulation with digitalis. The author generally orders for adults an infusion of the leaves. An accurate diagnosis of the condition causing the hemorrhage is necessary before the treatment is instituted. Focke (Therap. d. Gegenwart, Bd. lii, S. 306, 1911).

Large doses of digitalis are often tolerated by alcoholics, in particular those suffering from **delirium tremens**. In the latter state the not infrequent beneficial effect of the drug on the general condition, including that on

the delirium, appears to depend largely on the improvement in the circulatory functions.

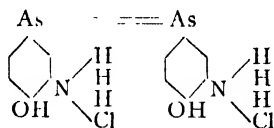
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AND

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Philadelphia.

**DIOXYDIAMIDOARSENOBENZOL** (arsphenamin; salvarsan; arsenobenzol; kharsivan; diarsenol; 606) is an organic compound of arsenic prepared by Berthelm, biologically tested in animals by Hata, and introduced into medicine in 1910 by Ehrlich, under whose direction the study of a long series of arsenical substances had been conducted. Dioxydiamidoarsenobenzol was in reality number 605 in this series; the compound dissolved in water, however, only with great difficulty, and it was therefore converted to the hydrochloride, *i.e.*, dioxydiamidoarsenobenzol dihydrochloride, or 606, the molecular formula of which is  $C_{12}H_{12}N_2O_2As_2 \cdot 2HCl$ , and the graphic formula:—



In addition, for each molecule of the compound there are present, in arsphenamin as commercially supplied, two molecules of water.

Dioxydiamidoarsenobenzol hydrochloride occurs as a fine, yellow powder, soluble in water, in methyl alcohol and in glycerin, less easily soluble in ethyl alcohol (1 part in 12), and insoluble in ether. When placed in water, the drug at first clumps together; shaking the mixture with glass beads is therefore a useful procedure to accelerate dissolution. The

resulting solution is acid in reaction. Before it is used sodium hydroxide is added to it to an extent sufficient to render it feebly alkaline. From this solution carbon dioxide precipitates the drug; this is the reason arsphenamin solutions gradually become turbid when exposed to the air.

Arsphenamin, moreover, even in solid form, easily becomes oxidized when in contact with the air for any length of time; the resulting substance is an oxide in which the two parts of the arsphenamin molecule are split asunder, the two mutual bonds of affinity between the arsenic atoms being now satisfied by oxygen. This oxide is about twenty times as toxic as salvarsan; a good preparation of the latter should not contain more than 0.5 to 0.8 per cent. of the oxide (Ehrlich).

**Neodioxydiamidoarsenobenzol** (neoarsphenamin; neosalvarsan; neoarsenobenzol; 914, etc.), introduced by Ehrlich in 1911, is a condensation product of salvarsan and formaldehyde sulphoxylate of sodium ( $H_2C \cdot OH \cdot OSO_2Na$ ), and may be represented graphically by replacing one of the hydrogen atoms united to nitrogen in the above formula by the group  $CH_2 \cdot OSO_2Na$ . This preparation has the pronounced advantages of dissolving at once when dropped in water and of yielding a neutral solution, so that the addition of sodium hydrate for purposes of neutralization is unnecessary.

In U. S. P. X (1926) these drugs became official as:—

*Arsphenamina* (arsphenamine), containing not less than 30 per cent. of arsenic. Dose, intravenous, 0.4 Gm.

*Neoarsphenamina* (neoarsphenamine), containing not less than 19 per cent. of arsenic. Dose, intravenous, 0.6 Gm.

Unfortunate results from injection of arsenical preparations may sometimes be due to poisoning by traces of the drug which remain in the syringe and in vessels for preparation of the solution from a previous injection and which have become oxidised by air exposure. The writer counsels very careful washing of the syringe and of the vessel in which the solution is made before each injection and before sterilization. In order to test for the presence of traces of the oxidised drug he submits the final washings to a chemical test, using a 2 to 4 per cent. solution of silver nitrate, which will reveal the presence of such minute traces as 1 in 100,000,000. With a solution of 1 in 100 of the oxidised drug the silver test solution gives an abundant, almost black precipitate, and with 1 in 10,000 a cloudiness and violet-brown color. In more dilute solutions there is still a characteristic coloration after a few seconds. Even after four or five washings he noted a reaction corresponding to 1 in 100,000. J. Golay (*Ann. de Derm. et de Syph.*, Sept., 1919).

The writer showed experimentally that shaking solutions of arsphenamine and neoarsphenamine in the presence of air led to marked increase of toxicity of the drugs. Preparations which are difficultly soluble should, for this reason, not be shaken as a dangerous increase in toxicity may result. Warning is given against preparing solutions in a mortar or large beaker. Roth (*Public Health Reports*, xxxv, 2205, 1920).

**DOSE.**—The dose of salvarsan for adults ranges from 0.2 to 0.6 Gm., the latter amount being the average full dose for a male subject, and the former used where dangerous complications are feared. The average full dose for female subjects is 0.5 Gm. The patient's general condition and the information obtained by physical examination should be taken into account in deciding upon the dose, the fact being borne in

mind, however, that the largest dose that can be administered without doing harm will, under most circumstances, give the best therapeutic results.

The writer, secretary of a commission appointed by the Cologne Medical Society, blames dosage for the fatalities. The number of deaths in 225,780 injections of arsphenamine, neoarsphenamine and arsphenamine-sodium totaled 20, 1 for every 11,289 injections. Twelve were certainly due to arsphenamine treatment, 5 were questionable, and 3 indirectly due to arsphenamine. All deaths from encephalitis were due to arsphenamine. The commission recommends that the maximal dose for men be placed at 0.6 Gm. and for women at 0.45 Gm., and that manufacturers be prohibited from putting up larger single doses than these. Meirowsky (*Munch. med. Woch.*, Apr. 23, 1920).

The dose of neosalvarsan is one and one-half times that of salvarsan.

Since the earlier years following the introduction of salvarsan and neosalvarsan there has been a tendency to reduce the dosage below that originally recommended. Administration of the full doses of 0.6 Gm. of the older drug, and 0.9 Gm. of the neo variety, is in many instances attempted only after 3 or more injections of smaller, ascending amounts.

**MODES OF ADMINISTRATION.**—The intravenous, intramuscular, subcutaneous, and rectal routes have all been employed in giving salvarsan. The first of these was soon found to be the best of all, and since it is that generally employed it will be described first. The subcutaneous method proved very unsatisfactory, and has been abandoned. The rectal method is of service in a limited number of cases. In

infantile syphilitic cases milk, both maternal and from the lower animals, has been used as a vehicle for arsphenamin.

In local diseases, mostly non-syphilitic, the drug is not infrequently applied externally.

**Intravenous Method.**—As already stated, arsphenamin as such forms a strongly acid solution, owing to the hydrochloric acid it embodies. This reaction must be changed before the compound is administered. The usual mode of procedure is as follows: About 30 to 40 c.c. of sterile physiological saline solution (0.9 per cent.), made from C. P. (chemically pure) sodium chloride and freshly distilled water, are placed in a sterile, graduated cylinder of 500 c.c. capacity. The graduate should preferably be provided with a ground-glass stopper, and may contain about 50 sterile glass beads, to facilitate dissolution of the arsphenamin by shaking.

The required dose of the remedy is then dropped in and the graduate agitated until the compound enters into solution. Neutralization is next effected by adding a 15 per cent. solution of pure sodium hydroxide in a certain specified amount, which varies according to the dose of arsphenamin used, as may be seen in the following table:

Dose of arsphenamin.	Volume of alkaline solution to be added.
0.6 Gm.	1.14 c.c. = 23 drops.
0.5 Gm.	0.95 c.c. = 19 drops.
0.4 Gm.	0.76 c.c. = 15 drops.
0.3 Gm.	0.57 c.c. = 12 drops.
0.2 Gm.	0.38 c.c. = 8 drops.

The addition of the sodium hydroxide leads to the formation of a precipitate, which redissolves, how-

ever, upon vigorous shaking. Enough saline solution is then added to make as many times 50 c.c. (or 40 c.c.) as there are tenths of a gram (0.1 Gm.) in the dose employed. Thus, if a 0.5-Gm. dose were being used, the solution would measure 250 c.c. (or 200 c.c.).

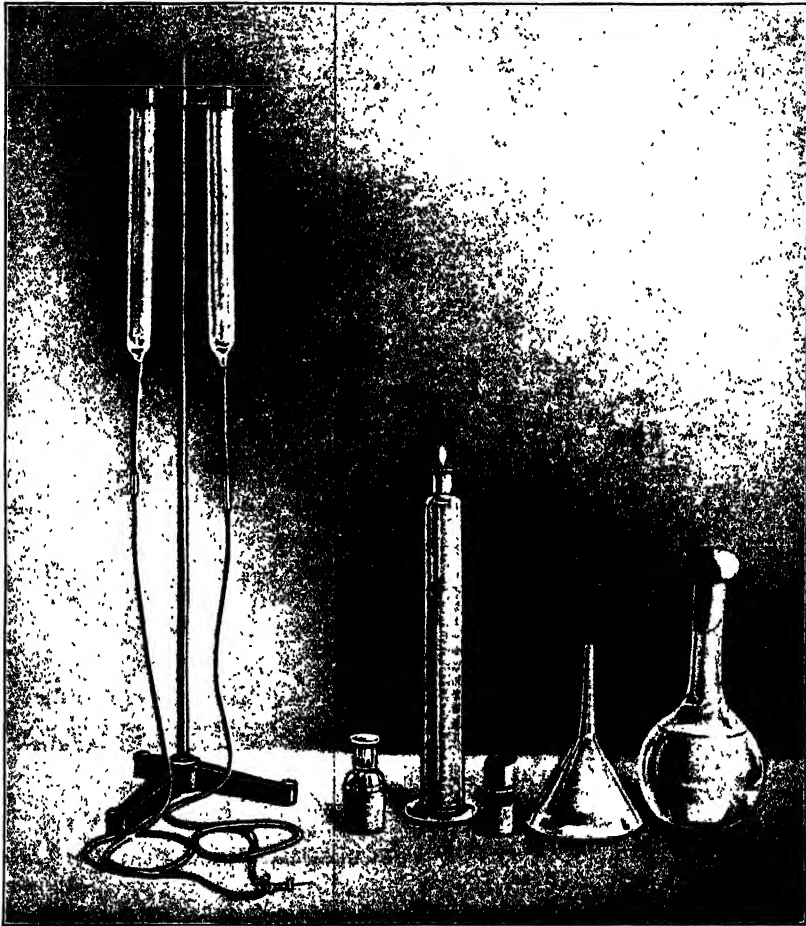
The finished preparation should be absolutely clear; if it is not, a few drops more of the sodium hydroxide solution should be added.

*Simplified Method for General Practitioner.*—One can prepare a solution of neoarsphenamin for use without any apparatus other than a sterile glass syringe and needle and 5 c.c. of sterile distilled water. The ampule is first shaken or knocked so that the powder flows easily and is not lumped. The tip of the ampule is then filed off, the opening in it being made large enough for introduction of the needle to be used. With the ampule almost horizontal, 5 c.c. of sterile distilled water are now introduced with the syringe. The ampule is next agitated for 30 seconds to a minute, when the powder should be in complete solution. To avoid spilling, the finger, covered with a rubber glove or finger stall, should be held over the tip of the ampule. Finally, the solution is drawn up into the syringe, and is ready for injection. If one desires to use more water, 5 c.c. or more of it can be placed in the syringe before sucking up the solution from the ampule. There is no greater liability to reactions with 5 c.c. than when more water is used. Great care must, however, be taken that the needle is in the vein. If in doubt, the tourniquet should be again applied and traction made on the piston; if blood freely enters the syringe, the needle is in the vein. At least 1 to 1½ minutes should be consumed in injecting the 5 c.c. The solution should never be used unless it is brilliantly clear. J. F. Schamberg (Jour. Amer. Med. Assoc., Jan. 15, 1921).

The solution may also be prepared by placing arsphenamin in a small sterile mortar, dropping the required number of drops of 15 per cent. sodium hydrate solution directly on to

the powder from a sterile pipette, triturating the powder and alkali with a sterile pestle or a thick glass rod with rounded ends, and pouring the resulting clear-yellow solution into a larger sterile receptacle containing the required number of cubic centimeters

by a clamp and leading to a stout hypodermic needle. The receptacle is hung or held at some elevation above the patient and the solution allowed slowly to run into the vessel. An advantageous variation from this, however, consists in the employment of



Assmy's apparatus for intravenous injection of salvarsan.

of sterile physiological salt solution (*e.g.*, 250 c.c. for a 0.5-Gm. dose).

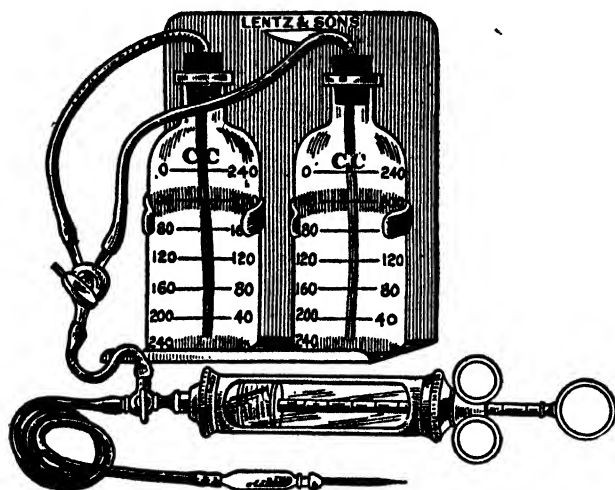
In administering the injection nothing more complicated is essential in the way of apparatus than a graduated 300-c.c. burette or even a funnel to the lower end of which is attached a piece of rubber tubing, closed below

two burettes or other receptacles, one for the salvarsan solution and the other for pure normal saline solution; the two tubes leading from these receptacles join in a three-way stop-cock, which permits of running into the vein either salt solution or salvarsan at will.

Some surgeons, Schreiber in particular, employ a large syringe. A more frequently used form of apparatus, however, is one similar to that shown in the annexed illustration, in which a three-way stop-cock is connected with the nozzle of a 20 or 50 c.c. Record or other glass and metal syringe. One of the rubber tubes attached to the two distal openings of the cock leads to the needle, while the other is connected with sal-

is exhausted, after which another syringeful of pure saline solution is drawn in and injected.

From experience in the treatment of 132 *infants and children* with congenital syphilis, almost all of whom received neoarsphenamin intravenously, G. Gelbjerg-Hansen (Ugeskr. f. Laeger, Oct. 11, 1923) concluded that infants are even more tolerant of the arsenical drugs than adults. The injections were usually given in a vein of the elbow or neck, or in the superior longitudinal sinus as a last resort. The dose



Apparatus for injection of salvarsan. The glass handle, connected with the needle through a slip-joint, acts as a guide in the insertion of the needle and receives the blood when the vein has been entered. (Cary.)

varsan solution and saline solution receptacles, or is left free so that its extremity can be dipped at will in either receptacle. The tube leading to the needle should be interrupted with a "window" of glass tubing or some other arrangement made so that any air-bubbles in the tubing may be seen before they can enter the vein. The syringe is first filled with saline solution and this injected, next the cock is turned so that the syringe can be filled with salvarsan solution, and successive syringefuls of the latter are injected until the dose to be given

was 0.075 Gm. below 3 months, 0.09 between 3 and 6 months, and 0.12 between 6 and 12 months.

In feeble patients, Weitgasser (Med. Klin., Jan. 27, 1924), to avoid pain, gives the drug intravenously in solution in 20 c.c. of a 50 per cent. solution of glucose.

Bernard has described a simple apparatus in which the force propelling the solution into the vein is obtained through compression of air, the device consisting essentially of a closed receptacle and a double-valved atomizer bulb. The container consists of a wide-mouthed bottle of 12-ounce (360 c.c.) capacity, provided with a rubber

stopper through which two glass tubes are passed, one reaching to the bottom of the bottle and the other, with which the bulb is connected, merely passing through the stopper. After preparation of the solution the latter is filtered into the bottle, which is meanwhile placed in hot water, to warm the solution as it drops in. In using the apparatus the first step is to remove all the air from the tubing by holding the latter vertically and compressing the bulb until a solid stream of fluid passes out through the needle. The tubing is then clamped and the needle inserted into the patient's vein, when the clamp is loosened and the fluid from the graduated bottle introduced into the circulation by pressure on the bulb.

Uhle and McKinney have devised an apparatus designated as the "vacuum burette." The burette is double-walled, and between the two walls is a vacuum which prevents loss of heat from the fluid placed in the inner lumen. Near the lower end of the rubber tubing attached to the reservoir is a thermometer. The needle used is of platino-iridium. The salvarsan is prepared by dissolution in 30 c.c. of normal saline solution at 118° F., neutralization being effected by the addition of 15 per cent. sodium hydrate solution drop by drop until the compound has been fully precipitated and redissolved. After running saline solution into the vein, the salvarsan solution is poured into the burette, and when it has passed into the circulation the receptacle and tubing are flushed with 10 c.c. of saline solution (Loux).

The vein into which the injection is made is either the median cephalic, median basilic, or the anterior radial

or ulnar vein—usually the first of these. The skin is first washed with green soap and water, then with sterile water and finally with alcohol. Some surgeons, after the cleansing with soap, lather and shave the part, apply tincture of iodine, wash this off with alcohol, then apply ether. A towel tourniquet or a bandage is next placed three or four inches above the elbow, in such a manner that it can be quickly undone, sterile towels clipped round the patient's arm, a prominent vein chosen, and the needle—a large one, preferably of platinum—passed directly through the skin into the distended vein. (In stout individuals or in children with small veins, the making of an incision or small V-shaped flap under local anesthesia and passage of the needle or a small cannula into the exposed vessel are sometimes necessary.) If the point is not in the vein, having either failed to penetrate or passed entirely through it, injection of a small amount of saline solution will at once cause visible infiltration and a slight swelling. If the needle has entered the lumen, on the other hand, blood will drop from it; or, if a syringe is being used, a little blood may be drawn out to make sure of the entrance, then immediately reinjected. (Occasionally a cannula, with trocar, is used instead of the needle, the trocar being withdrawn after the cannula has been introduced and the tubing from the salvarsan receptacle then attached, due care being taken to avoid the introduction of air; or, the needle attached to the tube may be fitted to the cannula, so that it can be slipped into it.)

Both indirect and direct administration should be employed when-

ever possible. Employing the intravenous route of administration in children, it will usually be found easiest to expose the vein before attempting to insert the needle. The dosage should be not less than 0.01 Gm. per kilogram of body weight. Repeated injections and supplemental treatment by mercurials may be necessary. The Wassermann reaction should be followed for a year. La Fétra (*Archives of Pediatrics*, Sept., 1912).

With the needle in position in the vein, it can be maintained there by a piece of gauze, tied around the rubber tubing and arm just above the needle. The tourniquet is next removed from the arm and some salt solution, at the proper temperature, allowed to run into the vein to make sure that no fluid will leak into the surrounding tissues. This precaution having been taken, the salvarsan solution is started. The patient meanwhile is recumbent. The injection of salvarsan should occupy five to ten minutes, and be interrupted for two or three seconds each minute (Martin). When it is concluded, sterile salt solution to the extent of 75 to 100 c.c. should be run in to wash all trace of the arsenic compound from the vein at the seat of injection, thus avoiding subsequent local irritation.

Do not infuse the solution into the vein too rapidly. It is best to have a needle of such capacity as will take eight minutes to introduce 200 c.c. of fluid. With the gravity apparatus the rapidity of inflow can be readily governed. Do not use glass pearls in the mixing jar, as small parts may chip off and cause embolism. Do not use a routine dosage of the drug, but gauge it according to the weight of the patient and the condition to be treated. Do not persist in intravenous injection if the patient shows signs of collapse during administra-

tion, but stop at once. J. F. Schamberg and N. Ginsburg (*Jour. Amer. Med. Assoc.*, Feb. 4, 1911).

Schreiber advises that if, during the injection of the salvarsan solution, leakage should occur, the skin becoming lifted up and the patient complaining of a burning sensation, a certain amount of bleeding should be allowed, as he has found this the best way to avoid infiltration of the tissues. Where the injection is completely successful the patient should experience no pain except that due to the small skin wound.

After the needle or cannula is removed, the patient's arm should be elevated and sterile gauze previously dipped in alcohol applied to arrest the bleeding. Collodion may then be applied to seal the wound, and a dressing of gauze, fixed with adhesive, terminates the procedure.

All apparatus should be sterile before use. Receptacles open at the top may be covered, before sterilization, with four or six layers of gauze, through which the sterile solutions may be poured into the receptacles immediately after these have been removed from the boiling water or autoclave. Burettes and similar receptacles may be sterilized instead with formaldehyde solution, followed by sterile water and alcohol.

The flask containing the sterilized distilled water for use in making the solutions should not be stoppered with cotton, but with gauze, as cotton fibers, falling into the fluid, might cause trouble. The best syringe for injecting is a glass Lürer of about 20-c.c. capacity. It should not have a metal plunger, as in that case the least blood may cause binding. Schreiber has a special needle made with a bayonet bend in the shaft, and on this bend a ribbed finger-hold.



The bayonet bend is to allow the needle to be more easily shoved along in the lumen of the vein. The arm is laid out on a cushion so as to lie flat and easy; a stout rubber tube is thrown around the middle of the upper arm and drawn tight enough to stop the flow of blood in the superficial veins, but not so tight as to impede the arterial supply, and fastened with artery forceps or a modern clip. It is very necessary that the arm should lie easy and still. Montgomery (Jour. Amer. Med. Assoc., Feb. 18, 1911).

The apparatus used by the writer is extremely simple. A large, heavy glass bulb-funnel, of about 500-c.c. capacity, without stopcock or stopper, is used as the receptacle. About four feet of small tubing is connected to this, with a pinch-cock and a large aspirating needle fitted to the distal end. A stopper graduate cylinder of 50-c.c. capacity, and a pipette of 2-c.c. capacity are also required. For the preparation of the solution of the drug, only one reagent is required, a 15 per cent. solution of sodium hydroxide in distilled water. No sodium chloride or hydroxide except the C. P. should ever be employed. The sterilization of the apparatus must be carried out by boiling in distilled water. The water used in making up the solution should be freshly distilled. The writer uses a simple combination of a Jena distilling flask and a Liebig condenser for this purpose.

The apparatus having been boiled for fifteen minutes in a covered dish with enough distilled water to cover the articles, the distilled water and sodium chloride solutions are put on to boil. These are conveniently contained in Erlenmeyer flasks, of about 500-c.c. capacity, with gauze stoppers. The saline solution is made up by adding 7.5 Gm. of C. P. sodium chloride to 1 liter of freshly distilled water.

About 20 or 30 c.c. of the hot sterile water is poured into the graduate, and the drug added to this. If the entire dose of 0.6 Gm. is not to be given, the deduction can most easily

be made by discarding a proper proportion of the solution. The stopper is placed in the graduate and the latter shaken until a perfectly clear solution results. The writer does not use glass beads.

Two c.c. of the sodium hydroxide solution are now added from the pipette, and the graduate shaken again. A voluminous precipitate results. More alkali solution is added drop by drop, with frequent shaking, until the solution again becomes clear. The approach of the point where the clearing occurs is indicated by a darkening of the liquid. An absolutely clear solution, with not even a trace of opalescence, should be had. Keeping the solutions hot will aid in obtaining and keeping this effect.

About 350 c.c. of the hot sterile salt solution are now poured into the bulb-funnel and allowed to run rapidly through the tube and needle for a few seconds, to be sure that all air is removed from the tube. It is even well to strip the tube through the fingers, to be sure that no air-bubbles remain.

The needle is now introduced into the vein, in the direction of the blood-current. The salt solution should be flowing constantly during this procedure, to prevent the access of air to the needle-end.

When it is seen that the salt solution is flowing satisfactorily, the salvarsan solution is carefully poured into the bulb. About fifteen minutes should be allowed for the 300 c.c. to run in. When the bulb is almost emptied, 50 or 75 c.c. of saline should be added, to wash out the tube and vein. H. L. Arnold (Jour. Mich. State Med. Soc., April, 1913).

The writer compares the results of 2 methods of administering arsenobenzol in 189 cases. The 89 cases treated by the concentrated course and the 100 cases treated by the prolonged course show the advantage to be with the prolonged course, because the reactions were less severe and the Wassermann became negative in more cases and with smaller doses, espe-

cially in secondary syphilis. H. E. Gibson (Brit. Med. Jour., Jan. 24, 1920).

A certain widely distributed brand of so-called pure gum rubber tubing seems to contain, when new, a toxic agent responsible for a definite type of reaction following the intravenous administration of arsphenamine, and possibly also of alkaline solutions and transfusion mediums. The toxic substance gradually disappears from the tubing on use. It is not destroyed by the ordinary sterilization by boiling, is insoluble in water, and is not apparently associated with the mechanically removable debris from the inner surface of the tube. It is apparently removable by soaking the tubing for 6 hours in normal NaOH solution and rinsing. The reaction induced by this toxic agent consists of chills coming on from 30 to 60 minutes after injection, with nausea, vomiting, diarrhea, a sharp rise in temperature, headache and lumbar cramps. Stokes and Busman (Jour. Amer. Med. Assoc., lxxiv, 1013, 1920).

The distilled water used for making the solutions should have been redistilled and then sterilized not longer than a day before the injection. The neck of the phial containing the salvarsan may be aseptitized by wiping with absolute alcohol, and the phial opened with the aid of a file previously sterilized in the flame of an alcohol lamp, but allowed partly to cool down.

The principal precautions to be observed in the administration of neoarsphenamine are: (1) Only a single ampule should be dissolved at a time. This drug must not be dissolved in bulk to be given to a series of patients. (2) Cold water only should be used. (3) The dilution should be not stronger than 0.1 Gm. ( $1\frac{1}{2}$  grains) of the drug in 2 c.c. (32 minims) of freshly distilled water. (4) A very small needle should be used, and injection take not less than 5 minutes.

U. S. Public Health Service (Reports, May 23, 1919).

Laxness in following the printed directions that accompany each ampoule of arsphenamine accounts for the greater number of reactions to treatment. One should note any departure from the normal lemon color of the brand of arsphenamine being used, and then immerse the ampoule in 95 per cent. alcohol for 15 minutes to detect obscure cracks. Cracked ampoules are to be rejected. Using the directed technique for one brand of arsphenamine while preparing the solution of another will, in some cases, cause reactions. Giving too large a dose of arsphenamine at the beginning of a course accounts for some reactions. Lack of preliminary preparation for a treatment—a laxative the night before and a light breakfast 4 or 5 hours before—is sometimes the cause. When 2 or more reactions occur from a multiple ampoule solution, in the majority of instances the fault will be found in the technique of preparing the solution, and the usual cause will probably be hypoalkalinity. Factors attributable to the patient, after both arsphenamine and the technique of preparing the solution have been excluded, include allergic idiosyncrasy, an inherited dominant susceptibility to arsphenamine medication; anaphylaxis, protoplasmic sensitization from repeated doses; blood synthesis reactions, in which arsphenamine becomes altered or precipitated from causes not understood, or ascribed to excess of carbon dioxide in the blood, or faultily prepared arsphenamine solutions; and the nitritoid reaction ascribed to the action of arsphenamine in destroying spirochetes and liberating large quantities of bacterial protein to which the tissues have become sensitized. J. F. Martin (Jour. Amer. Med. Assoc., May 1, 1920).

The needle employed for the injection should be of fairly large caliber, and preferably of platinoiridium or tantalum. Its point should be short

beveled, to diminish the risk of puncturing the vessel after the needle has once been inserted into it, but should also be very sharp, so that introduction through the skin will not require too much pressure.

*Neoarsphenamin*, dissolving readily in water to form a neutral solution, is prepared for injection by simply pouring into a sterile beaker 25 c.c. of freshly redistilled and sterilized water for each 0.1 or 0.15 Gm. of drug to be given, dropping the remedy in, and allowing it to dissolve, without stirring or shaking. Any turbidity remaining at the end of ten minutes means that the amount of water is insufficient. More fluid having been added, a clear solution will be formed provided the water is itself free of solid particles. Neoarsphenamin becoming rapidly oxidized on exposure to air, greater care is required to prepare the solution immediately before use than in the case of old salvarsan. Neoarsphenamin solution at body temperature should *not* be used, the water being heated, if unusually cold, only sufficiently to bring it to ordinary room temperature, *before* the neoarsphenamin is dissolved in it. The solution should at no time be agitated, as this favors oxidation. The same forms of injection apparatus are used as with arsphenamin. If scrupulous care is paid to the technique, most patients suffer no discomfort whatever from the injection, though some complain of a transitory metallic taste, and occasionally there is slight headache two or three hours later.

Emery observed fever after only 3 out of 600 injections of neo-salvarsan.

In *infants*, injections of neosalvarsan into the external jugular, epicranial, or

dorsalis pedis veins were successfully performed by the author in 100 cases. All injections were made without incision. Neosalvarsan was dissolved, whatever the dose, in 2 c.c. (16 minims) of twice distilled water. Three assistants were found necessary—2 to immobilize the head and trunk respectively (the child being also wrapped in a blanket), and the third to disinfect the field, etc. For injection in the external jugular, the child's crying efforts suffice to distend the vein. The needle, with *barrel filled* and attached, can usually be inserted easily into the vein. Blechmann (Paris méd., Jan. 31, 1914).

The increasing use of *neoarsphenamin*, according to Schamberg (Pa. Med. Jour., Jan., 1922), is due to the fact that it is better tolerated and distinctly safer. It is possible to cure virtually all cases of primary sero-negative syphilis with the arsphenamins alone. A high percentage of cases of secondary syphilis can be cured by weekly injections of arsphenamin or neoarsphenamin alone. Ten injections of arsphenamin appear, in general, to be equivalent to about 15 of neoarsphenamin. The majority of patients will tolerate 2 doses of 0.9 Gm. neoarsphenamin for 2 weeks and then once a week for 8 or 10 weeks, or longer. In primary syphilis, generalization of the infection may take place even though the Wassermann does not yield a positive reaction. Second, and at times third, courses are therefore advised.

Since the lead salts, alkaline silicates, calcium bicarbonate, magnesia, copper, etc., that may occur in distilled water prepared in unsuitable apparatus have proven responsible for some of the untoward effects noted after injections, Ravaut simplifies matters by administering neosalvarsan in the smallest possible quantity of water that will not produce hemolysis (through hypertonicity of the neosalvarsan solution), thus rendering unnecessary special precautions in the preparation of the water.

The author has recently been injecting as much as 0.9 Gm. of neosalvarsan dissolved in only 8 or 10 c.c. of distilled water. With this procedure, the neosalvarsan itself supplies the required isotonicity with the blood instead of sodium chloride. Distilled water prepared several weeks before and kept in ampoules of the highest quality glass can be used directly without causing any systemic reaction. The solution is prepared after the constricting band has been applied to the patient's arm and the skin cleansed with alcohol. The drug is merely dropped into the water, and the solution drawn up into the glass syringe through a special glass tube containing a small wad of cotton for purposes of filtration. The needle is then adapted to the syringe, air driven out, and the injection at once given. All rubber tubing is thus eliminated and a more strict asepsis rendered possible. The whole procedure of preparation and injection occupies only two minutes. The author has given 420 such injections without the least untoward result. Ravaut (*Presse méd.*, April 2, 1913).

Necessities of military practice led the author to simplify his technique as follows: A 2-c.c. (32 minims) glass syringe, good hypodermic needle, and a little absorbent cotton are boiled for 15 minutes in water as clean as is conveniently procurable. Then, compressing the cotton on the bottom of the receptacle with the outlet of the syringe, water is slowly drawn up, filling the latter. The syringe is allowed to cool completely, as warm water decomposes arsenobenzol. The cooling is accelerated by dropping ether on the syringe barrel. The vial containing the drug is then opened and the water projected into it drop by drop, the vial being meanwhile shaken. When the drug is completely in solution the fluid is drawn up into the syringe through the needle, and the intravenous injection given slowly. Doses of 0.3 to 0.9 Gm. of neoarsenobenzol were found to dissolve perfectly in the small amount of fluid, and were well toler-

ated provided due rapidity of preparation and slowness of injection were observed. P. Ravaut (*Presse méd.*, Oct. 11, 1915).

*Preparation of Patient for Injection and After-treatment.*—Some surgeons advise that where, as is usually the case, the volume of salvarsan solution introduced is about 250 c.c., and saline solution is employed in addition, the patient's blood-pressure should be lowered by the administration of an aperient on the evening before injection, so that the circulation will not be overloaded with fluid by the injection. The patient should have only a light breakfast on the morning of the injection, though after it ordinary meals may be taken unless fever occurs, when a milk diet should be temporarily imposed.

Rest in the recumbent position for at least two hours should be advised after injection.

The patient should not take solid food for 3 or 4 hours before the injection, and it is advisable to order an aperient, such as magnesium sulphate, the previous night. The author finds the "concentrated" method of giving neoarsenobenzol superior in every way to the "dilute" method. There are seldom any symptoms of reaction. He generally gives a preliminary course of 6 injections of 0.6 Gm. at intervals of a week, increasing the dose to 0.9 Gm. if necessary, with due regard to contraindications. In middle-aged patients, it is advisable to begin with 0.3 or 0.45 Gm., and prolong the intervals between administrations to a fortnight or more.

Ten or 12 weekly intramuscular injections of mercury are given simultaneously. A course of potassium iodide is then given, followed by mercury by the mouth for another 3 months. S. E. Dore (*Pract.*, Oct., 1918).

Phlebitis and thrombosis in the injected vein should be carefully watched for; if trouble of this nature arises, the limb should be kept absolutely at rest and fomentations of lead-water and laudanum applied.

Importance of investigating the circulatory system previous to the administration of salvarsan emphasized. The blood-pressure should be estimated; if such pressure is high, 180 or over, then one should carefully observe the patient for some time before administering the drug. If he is plethoric, it will do no harm to bleed him, removing at least an equal volume of blood to the total volume of salvarsan solution—about 250 c.c.

A differential blood-count should be made before and after using salvarsan, for it will give much information should complications arise.

The urine should be observed for a couple of days after salvarsan; some patients may show a trace of albumin that is transient and rapidly disappears, while others will complain of highly colored urine for several days, which is due to urobilin. J. L. Boehm (Amer. Pract., Aug., 1912).

The writers have given 3150 injections of neosalvarsan or novarsenobenzol Billon, dissolved in an amount of water never exceeding 2 c.c. Novarsenobenzol dissolved very quickly upon addition of the water to the drug contained in the ampoule. Neosalvarsan did not dissolve so readily, and care should be taken to distribute it in a thin layer over the lateral walls. Distilled water was used to make the solution, but when not available, boiled filtered water was used without any untoward reaction. The concentrated solution is well borne, and the authors have observed no vein irritation. Faure and Marsia (Presse méd., xxii, 221, 1917).

**Intramuscular Method.**—Intramuscular injections are given either in the buttock, in the lumbar region, or in

the trapezius muscle. More or less pain generally follows, and this route is therefore less acceptable from the patient's standpoint than the intravenous. In some cases, moreover, the drug becomes more or less completely encapsulated and, as a result, is only partially absorbed.

The gluteal muscles have been most used for intramuscular injections. The upper outer quadrant is best. Another site is the extensor spina muscle in the lumbar region. Meltzer has advocated the use of this region because absorption is more rapid, pain is less, and no large nerve-trunks can be involved: Place the patient face downward on the bed, draw a line between the posterior superior iliac spines, select a point about half an inch above this line and one to one and one-half inches from the midline. Insert the needle (which should be about three inches long) at right angles to the long axis of the body until it has passed through the dense lumbar aponeurosis, which can be easily felt. After the needle is well in the muscle, turn it parallel to the long axis of the body and toward the ribs, and insert it nearly to the base. H. F. Swift (N. Y. State Jour. of Med., June, 1911).

The writer warns against incising the toxic edema sometimes resulting from intramuscular salvarsan injections. Incision is indicated if an obvious abscess forms, when acute pain is noted. Alternate hot and cold applications give much relief. The redness which appears with the swelling quickly disappears under the following lotion:—

*R. Plumbi subacetatis* gr. x (0.6 Gm.).

*Aqua ammoniac*

*fortioris* ..... m v (0.3 c.c.).

*Alcoholis* ..... 5j (4 c.c.).

*Liquoris aluminii*

*acetatis* (N. F.) 3iij (12 c.c.).

*Aqua* ..... q. s. 5j (30 c.c.).

M. ft. lotio. J. E. R. McDonagh (N. Y. Med. Jour., May 3, 1913).

The remedy may be given (a) in an alkaline solution such as that used for intravenous injection; (b) in a neutral suspension; (c) in oil.

The *alkaline solution* may be prepared in the same manner as has already been described with the exception that only enough water is added to make 20 c.c., though some surgeons use 40 c.c.

Another estimable plan is first to place the salvarsan in alcohol (ethyl) —0.5 c.c. for each 0.1 Gm. of the powder, add 20 c.c. of warm sterile water, stir with a glass rod until the drug is wholly in solution, then add, while mixing, 1 c.c. of a decinormal (4 per cent.) solution of sodium hydroxide for every 0.1 Gm. of salvarsan.

Pain and induration from salvarsan injections are due to the sodium hydrate. The author now uses a 2 per cent. solution of sodium hydrate. He first puts the 0.6 Gm. of salvarsan in a 25-c.c. graduated cylinder, and dissolves it in 8 or 10 c.c. of hot water. The sodium hydroxide is then added in small quantities until a clear solution is obtained, care being taken not to add any sodium hydrate in excess. Hot water is then added in sufficient quantity to bring the total solution up to 20 c.c.; 10 c.c. of this solution are injected deeply into the buttocks on either side. Great care should be used to keep the injected fluid out of the adipose tissue. The sodium hydrate solution should be sterilized before each injection. B. C. Corbus (Jour. Amer. Med. Assoc., April 29, 1911).

Intramuscular injections of acid reaction exert a more continued effect than intravenous medication, which, though more convenient and painless, permits rapid excretion of the drug. The intramuscular introduction is advisable where contraindications (heart lesions, cerebral lesions) exist. P. Ehrlich (Münch. med. Woch., Nov. 21, 1911).

The author has given intramuscular injections of neosalvarsan in a dilution as high as 30 c.c. of water per 0.1 Gm. and noted severe pain and local swelling following. The pain seems to vary in proportion to the amount of fluid used, and as a dilution of 5 to 10 c.c. causes much less pain and local swelling, and does not increase the local or general toxic effects, the author employs that degree of concentration. The injections are made in the gluteal or lumbar regions, usually half in each side. The part is previously sterilized by painting with tincture of iodine. The author gives four injections of 0.9 Gm. at weekly intervals.

After about twenty-four hours there develops at the site of injection an induration, which usually is not tender to touch, or an edema, which is painless and pits upon pressure. This lasts for a few days and gradually disappears. If desired, the pain can be lessened by an injection about five minutes previously of novocaine or alypin solution. Rytina (N. Y. Med. Jour., June 29, 1921).

Arsphenamin compounds dissolved in serum dialyze less rapidly than in salt solution. But the difference is not sufficient to disprove their disappearance from the blood by simple diffusion into the tissues. Schreus and Wieler (Klin. Woch., May 14, 1925).

A *neutral suspension* of salvarsan is likely to produce less pain than an alkaline solution. It is made by adding to the salvarsan just enough sodium hydroxide to neutralize the two hydrochloric acid molecules in combination with it; the resulting free base is insoluble and can therefore only be given in the form of a suspension or emulsion. The necessity of adjusting the preparation to the neutral point renders this method more difficult to carry out than that with an alkaline solution. The salvarsan is mixed in a mortar with 1 c.c. of a saturated so-

dium hydroxide solution and the product dissolved in 4 c.c. of hot water. Three drops of a solution of phenolphthalein in alcohol are then dropped in. Glacial acetic acid is next added in successive drops until the preparation changes in color from red to yellow, and, finally, one or more drops of the sodium hydroxide solution added until a pink color again begins to appear.

A simpler method of preparing the neutral emulsion is that of Citron, who adds to the salvarsan 1 c.c. of absolute alcohol and 5 c.c. of hot water, and stirs until complete solution has been effected. Finally, 40 drops of a 10 per cent. solution of potassium bicarbonate are mixed in, and the preparation gently agitated with a glass rod until a very fine suspension or emulsion results.

*Oily preparations* of salvarsan are still advised by some, though it seems to be the opinion of many that the therapeutic effects are less marked than with the alkaline solution. Some claim it as an advantage, on the other hand, that the subsequent pain is relatively slight. Various menstrua have been recommended. Kromayer rubs up the drug with paraffin oil (liquid petrolatum) so that every 1 c.c. will contain 0.1 Gm. of the remedy, and administers fractional doses of 0.1 to 0.2 on alternate days; he asserts that if the injections be made slowly, pain and swelling will rarely, if ever, follow. Burke gives the drug in an olive-oil mixture containing 10 per cent of anhydrous wool-fat; enough of the menstruum is rubbed up with the salvarsan to make a mixture that will pass through the needle, and 4 or 5 drops of the U. S. P. 5 per cent. sodium hydroxide solution then

added, breaking down the lumps so that the emulsion becomes a soft mass. Lydston suspends the salvarsan in from 3 to 6 c.c. of 10 per cent. iodized oil of sesame.

Hazen employs an oil of the following composition:—

*R. Camphora.*

*Guaiacolis* . . . . . 3ss (2 Gm.).

*Petrolati liquidi*, q. s. ad 3j (30 c.c.).—M.

Just enough of the oil is used to make a fine, smooth emulsion—usually about 5 c.c.—the salvarsan being first placed in the mortar, previously boiled and allowed to dry, and the oil then added drop by drop, the mixture being meanwhile carefully ground.

The technique of an oily injection is simple. All that is needed in addition to the oil and salvarsan is a suitable syringe and a small mortar and pestle. A 5-c.c. syringe may be used, but one in which the end of the plunger is cut off square, and not round, as in the latter case some of the emulsion may work up between the plunger and barrel of the syringe and jam. The portal of exit of the syringe should be large, and a needle of from 17 to 20 gauge used. About 0.5 c.c. of air is injected along the needle so as to prevent the oil from escaping into the subcutaneous tissues. The injections may be made into either the gluteal or lumbar muscles. A small injection of 0.3 Gm. gives even less trouble than a full injection; so it is wise to give two half-doses at one sitting rather than a full dose. The results have been about the same as with the other types of intramuscular injection; most of the secondary skin manifestations and all the mucous patches, condylomata, and throat ulcerations cleared up speedily, while some of the tertiary lesions did very well and some were uninfluenced. Hazen (*Wash. Med. Annals*, Sept., 1912).

In executing any of the intramuscular or subcutaneous procedures, due

aseptic precautions should be taken, the syringe and needle being boiled, sterile receptacles, including the mortar and pestle, used, and the skin disinfected. Where an oily preparation is to be used, a needle of wide caliber—17 to 20 gauge—must be employed, and both the syringe-body and the needle must be absolutely dry. Hazen advises that after being boiled they be cleaned with alcohol and ether, or, better, that they be sterilized by dry heat. The preparation to be injected should always be freshly made, as salvarsan becomes partly oxidized on standing, with the formation of more toxic derivatives.

Great care is to be taken, in injecting an oily preparation or suspension, that none of the fluid gets into a vein. The simplest plan is, after inserting the needle, to wait a short period before connecting the syringe-barrel with it, to see if any blood exudes. Burke recommends that one syringe be half-filled with the oily menstruum unmixed with salvarsan, and the piston be drawn upon, making suction on the oil. If a vessel has been punctured the oil will be blood-stained, in which case the needle should be taken out; if it is not, the first syringe is detached and replaced by another containing the salvarsan mixture. After the injection is finished the salvarsan syringe may be replaced by the pure-oil syringe and a little oil injected, to avoid leaving a trail of salvarsan along the needle-track. The needle should be withdrawn quickly, pressure being made at the same time over the site of injection.

*Neosalvarsan* may be given intramuscularly either in sterile water,

saline solution, or glycerin. Theoretically, it should be superior to salvarsan owing to the fact that a neutral solution can be administered. Nevertheless neosalvarsan injections have proven decidedly irritating, causing transitory pain, inflammatory swelling and edema at the point of introduction. As in the case of salvarsan, therefore, intravenous administration of neosalvarsan is preferred by nearly all who have used the two methods. Hazen himself prefers the intravenous route to the oily injections. For intramuscular injection a solution in 5 to 10 c.c. of sterile water is most employed. The use of 0.4 or 0.5 per cent. saline solution is disadvantageous in that turbidity results, and according to Schreiber the preparation becomes more toxic. Absorption of neosalvarsan is more rapid than with salvarsan, and less local induration is caused.

The authors treated 2 parallel series of cases of **syphilis**, the 1 with intravenous injections of salvarsan or its substitutes, the other with deep subcutaneous or intramuscular injections of neosalvarsan or its substitutes, and found the subcutaneous or intramuscular method distinctly more efficient than the intravenous in both primary and secondary stage cases, though slightly better results seemed to follow the intravenous method in tertiary cases. Hypodermic administration was decidedly more effective than intravenous in producing a negative Wassermann reaction. The drug being more slowly absorbed and eliminated, the tissues are kept effectively saturated. The alarming side actions are almost wholly absent. To obviate pain neosalvarsan is best given subcutaneously or intramuscularly in a solution of 0.6 Gm. (10 grains) in 1 c.c. (16 minims) of 4 per cent. stovaine, to which 1 c.c. (16 minims) of creocamph cream is



added and the whole well shaken. The solution is prepared in the syringe. Harrison, White and Mills (Brit. Med. Jour., May 5, 1917).

**Subcutaneous Method.**—The pain and local necrosis caused by subcutaneous injections of salvarsan are so marked that this procedure has been largely abandoned. Neosalvarsan was found by McIntosh and Fildes to be practically painless when injected only in the dose of 0.1 Gm., but necrosis of the subcutaneous tissues nonetheless resulted. The epifascial method of W. Wechselmann is a modified subcutaneous procedure by virtue of which the difficulties referred to are partly obviated.

Although experience with arsphenamin and its congeners has led to the well-nigh universal use of the intravenous method in preference to all others, a few observers are still disposed to lay stress on certain asserted advantages of the *subcutaneous route*. Thus, according to Minet and Legrand (Rev. de méd., Apr., 1922), subcutaneous injections of neosalvarsan are advantageous in being simple, in producing no shock, syncope, nor late reactions, and in permitting the use of relatively large quantities of the drug. They are made on the outer aspect of the thigh, in the trochanteric region and over the fascia lata. The needle must be moved about in order to make certain that it is perfectly free. Its point must be in the subcutaneous fat. The neosalvarsan must be dissolved in not more than 0.5 to 1.5 c.c. of the solvent, and the injection must be made rapidly, to avoid oxidation and consequent pain. Glucose and phenol, in solution, constitute the solvent. These writers have injected as much as 0.45 Gm. daily without untoward result. The usual dosage is 0.05, 0.10, 0.15, or 0.30 Gm. Fifteen daily injections are given, followed by 15 days' rest. The arsenical treatment is coupled with mercury biniodide or benzoate. During the rest intervals, large doses of potassium iodide are also given. The results are asserted to have been highly gratifying. On the other hand, G. Milian (Bull. et mém. Soc. méd. d. hôp. de

Paris, Feb. 9, 1922) has reported instances of serious and even fatal results following hypodermic injections of arsenobenzol, and maintains that such injections are attended with the same risks as intravenous administration.

**Rectal Method.**—This is doubtless a somewhat imperfect and probably uncertain mode of administration which should be employed only under exceptional conditions. The most pronounced results are not to be expected from it.

Weill, Morel, and Mouriquand have advised its adoption in children, in whom intravenous injections are not easily given, *e.g.*, in cases of severe chorea, inherited syphilis, anemia, etc.

In some children from 10 to 13 years of age successive doses of 0.10, 0.20, and 0.40 Gm. of salvarsan were given by rectum. The drug was prepared as though for intravenous injection, mixed with about 100 c.c. of 0.5 per cent. salt solution and 5 or 10 drops of laudanum, and slowly administered through a tube introduced as deeply as possible into the rectum. Care was taken to have the fluid retained at least four hours. In each case treated pronounced improvement was noted. Barring emergency cases, rectal administration is the method of choice for giving salvarsan to children, since along with sufficient activity of the drug there is an entire absence of unpleasant reactions, local or general. Weill, Morel, and Mouriquand (Lyon méd., July 7, 1912).

When mercury fails, or exceptionally prompt action is necessary, giving arsphenamin by the enteroclysis method offers superior advantages in children. The author uses a 20-c.c. syringe and small Nelaton catheter. The bowels are emptied first, when possible, and the child constipated with paregoric, or 1 or 2 drops of laudanum are added to each injection. Notwithstanding large doses, there was never any appreciable reaction,

and soon marked improvement was apparent. The children were given usually about 6 intrarectal injections of doses of from 0.05 to 0.1 Gm. ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains) at 5- or 8- day intervals. The injection was generally retained from 6 to 8 hours. S. Araujo, Jr. (Brazil-Medico, Aug. 3, 1918).

Intrarectal administration of arsenophenamin or neoarsphenamin recommended in cases in which the intravenous method is not possible or requires the exposure of a vein by incision. The drug is prepared as for intravenous injection, but only 25 to 50 c.c. ( $6\frac{1}{4}$  to  $12\frac{1}{2}$  drams) of fluid are used for neoarsphenamin and about 100 c.c. ( $3\frac{1}{2}$  ounces) for arsenophenamin. The patient is put to bed and the solution run into the rectum slowly, over a period of about 10 minutes. The patient is encouraged to retain the injection, and the hips may be elevated or the foot of the bed raised to facilitate retention, especially in children. A cleansing enema may be given before the injection, but is not always necessary. The injections can be given every 3 days, the full dose of 0.9 Gm. of neoarsphenamin and 0.6 Gm. of arsenophenamin being used for adults and one of 0.1 Gm. for each 25 pounds of body weight for children. Boyd and Joseph (Jour. Amer. Med. Assoc., Aug. 17, 1918).

The night before an injection the patient is given a mild laxative, and next day takes one light meal. A copious tepid irrigation is given, followed by a pill of 0.01 Gm. of opium. The novarsphenobenzol is dissolved in 50 c.c. of freshly distilled water and injected with a sterile glass syringe and catheter. Grajewski (Urol. and Cut. Rev., Jan., 1919).

Administration *by the rectum* was studied in 8 children, 0.3 to 0.6 Gm. of neoarsphenamin being used. Arsenic appeared in the urine to the extent of 0.15 to 0.34 per 1000, as compared to 2.53 per 1000 after a dose of 0.15 Gm. given intravenously. Retention of the enema is, of course, a prerequisite to absorption, and opium seemed of little

assistance in this connection. Noeggerath and Reichle (Arch. f. Kinderh., July 21, 1923).

**Oral Method.**—The oral route has been successfully used by Schamberg, Kolmer and Raiziss.

One-half grain (0.03 Gm.) of arsenobenzol in enteric capsules was given after each meal to about 30 patients in various stages of **syphilis**. Usually it required about 3 weeks to cause disappearance of a secondary macular or papular eruption, but in 1 case a large papular syphilide of the face disappeared in 3 or 4 days. Tertiary nodular lesions also required 2 to 3 weeks. To prevent oxidation of the arsenobenzol in the capsule, sodium hydrosulphite was incorporated with it, and a small amount of bismuth subgallate added to prevent diarrhea. Inaccessibility of veins through excessive adiposity, thrombosis of veins due to repeated injections, or similar reasons preventing intravenous injections, justify oral use of salvarsan, which is also indicated as a supplementary treatment to intravenous use, to keep the drug continuously supplied to the blood. In oral treatment of syphilis salvarsan is preferable to mercury. Schamberg, Kolmer and Raiziss (Jour. Amer. Med. Assoc., Dec. 23, 1916).

Administration of arsenophenamin *by the mouth* was tried out by the writer, 0.4 to 0.55 Gm. being given every 2, 3 or 4 days to a total of 2 to 6 Gm. The treatment, however, proved unreliable. A. Renault (Bull. Soc. méd. des hôp., Mar. 9, 1923).

**Intraspinal and Intracranial Methods.**—In treating the late manifestations of central nervous syphilis, direct application of the remedy to the nervous tissues has seemed desirable. Injection of neosalvarsan into the spinal canal has been tried, but fatal results occasionally followed.

An improved method is the intraspinal injection of salvarsanized blood-serum introduced by Swift and

Ellis. An intravenous injection of neosalvarsan is given, and blood withdrawn from the patient an hour later. As described by another observer who used salvarsan instead, as soon as the blood is withdrawn the fibrin is whipped out and the blood diluted with an equal amount of physiologic salt solution. This is left in the ice-box over night, the serum removed the following day and heated at 56° C. for ½ to 1 hour. The intraspinal injection is made with an ordinary glass cylinder, a small rubber bulb being attached to the lowest arm of a glass T, so as to make slight pressure when needed. The interval before withdrawal of blood was sometimes shortened to ½ or ¾ hour. Thirty c.c. (1 ounce) of 50 per cent. serum was taken as the standard dose, an approximately equal amount of spinal fluid being withdrawn. The usual interval between treatments was 2 weeks. Six of 11 cases of *paresis* showed improvement. L. B. Pillsbury (Jour. Amer. Med. Assoc., Oct. 10, 1914).

Intraspinal arsenobenzol treatment is attended with little or no danger if ordinary care is exercised in preparing the serum. Many late and apparently hopeless cases were arrested by this treatment. Arsenobenzol intravenously is very efficient in superficial nervous involvement manifested by headache, slight cranial nerve palsy, and luetic vascular conditions, but in the resistant affections formerly termed metasyphilis, the intraspinal method, systematically and judiciously employed, is far superior. Ogilvie's technique is used by the author, but the dosage never exceeds 0.5 milligram (½<sub>2</sub> grain), and is preferably limited to 0.3 milligram (½<sub>20</sub> grain). The serum should be used immediately, or certainly not later than 3 hours after its withdrawal. No spinal fluid is withdrawn unless it is under considerable pressure. The patient is kept in bed without pillows and with the foot of the bed elevated for 24 to 36 hours. The treatment is repeated until the

Wassermann is negative and the cell count and globulin normal. After apparent cure these tests should be renewed several times a year for a number of years; any slight positive tendency indicates further treatment. The author reports 6 cases, including 2 of early paresis, in which the treatment resulted in clinical and serological recovery. B. R. Tucker (Va. Med. Mthly, May, 1918).

Of 14 cases of *paresis* treated by intracranial injection of salvarsanized serum, 5 improved enough to return to work, and were still well after 7 to 11 months. At the end of 11 months, 1 patient had a bad relapse, but he responded immediately to additional treatment. Wardner (Amer. Jour. of Insanity, Apr., 1916).

Administration by way of the *inferior turbinates* is feasible. The solution having been slowly injected into the spongy tissue of the turbinate, the needle is allowed to remain *in situ* a few seconds before withdrawal, after which a small tampon of iodoform gauze with petrolatum is applied to check the bleeding. The tampon is permitted to remain until the next day. Podestá (Semana med., July 24, 1924).

**External Application.**—Various kinds of ulcers, including those of syphilis, chancroids, Vincent's angina, may be advantageously treated externally with a mixture of salvarsan or neosalvarsan and some bland substance such as bismuth subnitrate.

In a case of **parenchymatous keratitis** energetic mercurial treatment had not prevented the extension of the process to the second eye. The author applied a little neosalvarsan in powder to one eye and instilled a few drops of a 2 per cent. solution into the second eye. The extension of the process was at once checked in both eyes and the cornea soon commenced to clear up. It may be of advantage to apply the neosalvarsan suspended in an oily solution of atropine, as decomposition of the drug is prevented in this way. L.

Rosenmeyer (Münch. med. Woch., Nov. 5, 1912).

Observations indicating how the untoward effects of salvarsan, when locally applied, can be avoided: Mix the compound with liquid petrolatum in the proportion of 1 part of salvarsan to 10 of petrolatum. The best results were obtained by using neo-salvarsan in the same manner. It seemed to produce less irritation than salvarsan and not to coagulate albumins. It penetrates more energetically the pathological tissues. Cicatrization of **soft chancre** was found to occur very rapidly at first, the healing process then becoming less active. Nevertheless, even large, soft phagedenic processes yielded in from six to twelve days. Melun (Thèse de Paris, 1913; N. Y. Med. Jour., April 5, 1913).

**CONTRAINDICATIONS.** — Salvarsan is usually contraindicated in the presence of severe non-syphilitic visceral diseases, especially those affecting the heart, kidneys, and liver. In cases of aneurism, the injection of the remedy is considered hazardous, though certain French clinicians have used salvarsan in this condition with asserted good results. Well-compensated valvular lesions in young subjects do not contraindicate it. In syphilitic myocarditis there is some risk, but good results may be obtained with small doses. Arteriosclerosis is a relative contraindication, more particularly where the intracranial vessels are involved, as the rise of intracranial pressure and local reaction produced may lead to hemorrhage.

Syphilitic aortitis complicated with heart-muscle degeneration—especially the triad, syphilitic aortitis, sclerosis of the coronary arteries and myocarditis—forms an absolute contraindication against the use of salvarsan. **Angina pectoris** without com-

plication of heart muscle is most favorably influenced by salvarsan. K. Martius (Münch. med. Woch., May 16, 1911).

Salvarsan is chiefly indicated where changes in the heart muscle are still reparable and slight. In the tertiary stage, bradycardia would be an absolute contraindication, while with tachycardia a cicatrix may not yet have formed, so that the chief lesion is still a gummatous infiltration. It must be remembered, however, that the rapid absorption of gummatous tissue may leave a weak spot in the walls of the heart which might rupture. Salvarsan is absolutely contraindicated in acute rheumatic endocarditis, severe non-specific myocarditis, and severe cardiac complications of kyphoscoliosis, Basedow's disease, goiter, emphysema, lung affections, non-specific arteriosclerosis, and nephritis. It is indicated, however, in the early stages of lues, where the chief symptoms are arrhythmias, tachycardia, palpitations, dyspnea, anginal symptoms, accidental murmurs without endocarditis, aortic insufficiency, provided there is no pronounced dilatation or functional insufficiency. In tabes or general paresis with heart or arterial disease, the drug should not be employed. M. Breitman (Berl. klin. Woch., Sept. 25, 1911).

Albuminuria, if not marked, is not held to be a contraindication, as it may be due to the syphilitic infection, and be actually benefited by the remedy. Caution as to dosage is, however, necessary in these cases. The presence of casts in the urine is a contraindicating circumstance. Diabetes is likewise a contraindication, though sometimes glycosuria in syphilis is the result of syphilitic catarrh of the pancreas. Nixon, referring to the fact that the urine should always be examined before giving an injection, advises that one make sure in

particular that the quantity secreted is normal, the specific gravity within healthy limits, and, above all, that the excretion of urea is sufficient.

Where the liver is in a pathological state, salvarsan will tend to accumulate therein more than if it is normal, and is likely to cause additional destructive changes in the cells, whence acute yellow atrophy may develop. Catarrhal jaundice in early secondary syphilis is not a contraindication, but later, when jaundice is due to gummatous formations involving the parenchyma, the drug should not be given (McDonagh). In debilitated alcoholics, or those suffering from cirrhosis, salvarsan should not be employed.

In syphilitic disease of the central nervous system, particularly where there are signs of cerebral or spinal meningitis, psychic disturbances, optic neuritis, or epilepsy, special caution is necessary, and the dose given should not exceed one-half the usual amount. In cases of bulbar paralysis the drug had best be entirely withheld. It is to be borne in mind that with large doses the reaction is much more marked than with small. Especially at the beginning should the dosage be extremely guarded. Cases of general paralysis in which the diagnosis is obvious, late cases of tabes with negative Wassermann reaction, acute cases of cerebrospinal syphilis, and nervous disorders in congenital syphilis contraindicate salvarsan (McDonagh).

Following contraindications to salvarsan enumerated: (1) non-luetic diseases of the optic nerve and retina; (2) neuroses and organic diseases of the heart and blood-vessel., (3) severe diseases of the lungs, excepting tuberculosis if there is no hemop-

tysis; (4) severe non-luetic nephritis and diabetes; (5) severe visceral lues, ulcers of the stomach; (6) advanced degeneration of the nervous system and alcoholism; (7) severe congenital lues of the newborn; (8) febrile diseases of various kinds; (9) menstruation; (10) senile degeneration, non-luetic marasmus and cachexia. Stülpe (Klin. Monatschr. f. Augenheilk., March, 1911).

Persons with abnormal functioning of the thyroid are peculiarly liable to show intolerance to arsphenamine. Frequently, attacks of diarrhea in apparently healthy persons were soon followed by tremor and restless irritability; then came acceleration of the pulse and palpitations and—perhaps not until after a long interval—the thyroid began to enlarge and finally exophthalmos occurred. Be wary in case of attacks of diarrhea without apparent cause. Febrile reaction developing on the second day or later indicates intolerance. L. Lortat-Jacob (Prog. Méd., July 17, 1920).

Cases of pulmonary tuberculosis in the third stage should not be given salvarsan, as hemoptysis might result. Non-syphilitic epilepsy contraindicates salvarsan. Advanced age is also a contraindication.

Exclude from salvarsan treatment all those with depressed vitality from any cause other than syphilis, or who have signs of cardiovascular injury or kidney trouble, chronic poisoning from alcohol, nicotine or lead, or an infectious disease including florid syphilis itself. Especially dangerous are tuberculosis, severe gastro-intestinal disease and nervous affections with destruction of pathologic tissue. Luithlen (Therap. Monats., Jan., 1914).

#### PHYSIOLOGICAL ACTION.—

Our information on this subject is in a somewhat fragmentary state, the researches conducted having dealt chiefly with the lethal dose, the mode of elimination, the question of storage of salvarsan in various organs, and

its effects on the tissues from the histological standpoint.

**Toxicity.**—Kochmann found that intravenous injections of salvarsan in rabbits caused death only when the amount of elemental arsenic contained in the salvarsan introduced was 0.034 Gm., as compared with 0.00456 to 0.0053 Gm. of sodium arsenate. The toxicity of salvarsan is thus far lower than that of inorganic arsenicals. Kolmer and Schamberg found that salvarsan could be given by mouth in pills, capsules, or solution, in mammals, in the dose of 0.02 to 0.03 Gm. per kilogram of body weight without causing toxic symptoms. A dog was thus given 0.57 Gm. in the course of twenty-nine days without any disturbance resulting.

**Storage and Elimination.**—Salvarsan remains in the circulation for some time after intravenous injection, as was shown by Abelin in 1912 in a series of 8 human cases. Possessing apparently a selective affinity for certain tissues of the body, it—or some derivative—tends to collect in the liver and the kidneys. According to French investigators about three times as much arsenic is temporarily stored in the liver as in the kidneys. The question as to whether there is an affinity of the central nervous tissues for salvarsan, such that the drug might sometimes be directly responsible for untoward nervous phenomena in syphilis, has been fairly conclusively settled in the negative. Morel and Hugounenq, while they noted an evident “neurotropic” tendency in the case of arsenic acid, failed to find it with salvarsan. Beck, from experiments on mice, reached the conclusion that salvarsan exerts no

toxic effect upon the nerves of the head, including the auditory nerve.

Several cadavers of individuals dying of intercurrent affections from two weeks to several months after injection of salvarsan examined. In one cadaver two weeks after injection 6.5 mg. of arsenic was found in the liver; 3.1 mg. in the kidneys, and 1.8 mg. in the spleen. Bornstein (*Deut. med. Woch.*, Jan. 19, 1911).

Cerebrospinal fluid examined in 17 cases of syphilis to each of which 0.6 Gm. of salvarsan was given intravenously. The fluid was withdrawn at intervals of from fifteen minutes to forty hours after the injections. Doses up to 0.6 Gm., or perhaps more, do not ordinarily result in the presence of any arsenic in the cerebrospinal fluid. Arsenic is present in the fluid practically only when the dose is so large or so frequently repeated as to cause a meningoencephalitis, which is sometimes of a fatal character. Camp (*Jour. Nerv. and Mental Dis.*, Dec., 1912).

Experimental study in which the amounts of arsenic found in the brain, including the cerebellum, medulla, and cranial nerve-roots, after salvarsan, were no greater than in untreated animals, though in one instance the combined medulla and spinal cord showed a slight excess. Almost always large amounts—up to 0.14 per cent.—were found in the liver. The kidneys contained only a relatively small amount, sometimes only a trace. The bile and heart, in the one instance in which they were examined, showed 0.2 per cent. and 0.083 per cent., respectively. Mouneyrat had concluded that salvarsan was distinctly neurotropic. Morel and Mouriquand (*Lyon méd.*, Feb. 9, 1913).

About  $\frac{3}{4}$  of the arsphenamin given intravenously leaves the blood stream in a few minutes after completion of the injection, and the remainder is rapidly reduced in amount, though traces may still be found after 24 hours. The drug is stored in the liver, spleen, kidneys, lungs, and cardiac and

skeletal muscle. There is evidence that already 3 hours after injection the amount of the drug has been appreciably reduced by alteration, excretion or both. The liver is a more important excretory organ for arsphenamin and neoarsphenamin than the kidney. The brain shows a much lower concentration than any other organ. The cerebrospinal fluid during the first 24 hours, if it contains the drug at all, does so only in minute concentration. Kolls and Youmans (Johns Hopk. Hosp. Bull., June, 1923).

When injected into the muscles, salvarsan is only slowly and imperfectly *absorbed*. Neosalvarsan, according to Swift, is taken up much more rapidly, between 75 and 85 per cent. of the arsenic being absorbed in the first week—the remainder, however, quite slowly, so that at the end of six weeks 5 per cent. of the arsenic is still present in the injected muscle. Ullmann and Haudek already in 1911 emphasized, on the basis of X-ray experiments, the advantages, where salvarsan was to be administered hypodermically, of dividing the dose into several small ones given at different points, as only a small proportion of large doses was absorbed and the remainder merely injured the tissues at the point of injection.

The rate of absorption is most constant after the intramuscular injection of the neutral suspensions, a little more irregular after the injection of the alkaline solution, and most irregular after the injection of the acid suspensions. This is what might be expected if the rate of absorption is dependent upon the degree of injury produced by the injection, since neutral solutions inflict the least injury. During the first week after intramuscular injections of neosalvarsan as much arsenic is absorbed as after six weeks of salvarsan. Swift

(Jour. Exper. Med., vol. xvii, p. 83, 1913).

The *excretion* of salvarsan takes place chiefly through the kidneys, and to a less extent by the intestines, skin, and lungs. Its rapidity is subject to marked variations according to the mode of introduction. Escalton, studying the urinary elimination of salvarsan by means of Abelin's color reaction, found that the curve of excretion showed two maximal points, the first in the four or five hours just after the injection and the second twenty to twenty-eight hours or sometimes forty-eight hours after it. In the interval between the two summits of the curve, the excretion was markedly lessened and sometimes even at a standstill. The duration of the elimination and the total amount excreted were found to increase with each successive injection. According to Abelin the excretion of salvarsan begins in from five to fifteen minutes after an intravenous injection. Fischer and Hoppe found only traces of arsenic in the urine three days after the introduction of salvarsan by this route. That arsenic excretion is not always finished on the fourth day after intravenous use, however, was shown by Bornstein.

After intravenous injection of goats, the serum contains arsenic in a form which cannot be separated from the proteins by dialysis, and which is precipitated with the serum proteins by tannic acid ("bound arsenic"). No such combination is obtained when inorganic arsenic is injected. This combined arsenic is found in the blood long after all free salvarsan and neosalvarsan have been eliminated. It is found in the plasma and in the red cells, but no trace of arsenic is retained in the fibrin. W. J. Young (Biochem. Jour., Dec., 1915).

The author found considerable fluctuation of the arsenic content of the urine after salvarsan. The length of time during which arsenic may be found in the urine varies with the method of administration: In intravenous injection, from nine to sixteen days; in intramuscular, from twenty-five days to six months. In a nursing woman who received salvarsan, arsenic was found in the milk. Merkurjeff (Roussky Vrach, June 9, 1912).

The writers found in 12 nursing mothers that after intravenous arsenical medication the presence of arsenic in the *breast milk* is more constant than in either the blood or urine; arsenic is found in appreciable amounts long after its administration. The amount of arsenic received by a nursing infant in its feedings is probably sufficient to be of some therapeutic value. Energetic treatment of syphilitic mothers during lactation is, therefore, advisable. Fordyce, Rosen and Myers (Am. Jour. of Syph., Jan., 1923).

Differences of *excretion* between different members of the arsphenamin group. Tryparsamid is excreted rapidly through the urine, arsphenamin and silver arsphenamin very largely through the feces, and neoarsphenamin largely through the urine but mainly through the feces. A relationship between the late arsenical reactions and failure to excrete was also shown. Conditions such as jaundice or dermatitis may delay excretion. Fordyce, Rosen and Myers (Amer. Jour. of Syph., Oct., 1924).

Fischer and Hoppe showed that after intramuscular administration of salvarsan, somewhat less than one-half the whole amount can be recovered from the urine, and that the elimination is not complete for twelve days. In one fatal case arsenic was found in the gluteal muscles thirty-six days after the injection. It seems unquestionable that the local necrotic changes and partial encapsulation occurring after these injections exert a

marked retarding effect upon the absorption of salvarsan, and, in addition, that the rate of absorption and consequently the intensity of therapeutic action as well as the rapidity of elimination are subject to pronounced variations in different cases—another disadvantage of the hypodermic routes of administration as compared to the more direct intravenous method.

Arsenic can be found in some cases six and nine months after an intramuscular injection and as much as three months after an intravenous injection. Heuser (Med. Klinik, April 9, 1911).

Experiments made with gastric contents, feces, bile, and urine which demonstrated that within twenty-four hours after *ingestion* of salvarsan, arsenic may be found in both bile and urine. Probably only a portion is absorbed, and this is quickly eliminated. J. A. Kolmer and J. F. Schamberg (Jour. Exper. Med., vol. xv, p. 498, 1912).

**Effects on Circulation, Blood, and Urinary Apparatus.**—Salvarsan does not appear directly to depress the normal heart and blood-vessels to any marked extent. A temporary fall in blood-pressure and slowing of the heart rate has, however, been reported to follow its intravenous injection in some instances. Concerning its effects on the blood-cells the results of investigation have been contradictory. Normal kidneys, so far as is known, do not suffer from the presence of pure salvarsan, though where the drug has been allowed to undergo oxidation before use a tendency toward diminished renal activity or even anuria may be manifest.

In rabbits the author found that long-continued administration of salvarsan



intravenously brings about a slight nephritis. After toxic doses given during a short time, a marked fall of blood-pressure and serious renal insufficiency occurred, but lesions were not visible in the kidneys. Where nephritis had been previously excited by cantharidin, rabbits showed marked sensitization to salvarsan, whereas if the nephritis had been caused by mercury or chromic salts, that is, was essentially tubular, no ill results were obtained till large doses were employed. Animals with artificial tricuspid insufficiency, with resulting congestion of abdominal organs, bore salvarsan worse than others with aortic leakage. Alverens (*Arch. f. exper. Path.*, Bd. lxxii, 1913).

Influence on blood-pressure was studied by the writer in 100 cases in which the drug was given intravenously for syphilis, almost all cases being in the secondary stage. In 77 cases the injection was followed by a fall in both the systolic and diastolic pressures. The average fall of systolic pressure was 16 mm. Hg. and of the diastolic pressure 13 mm. Hg.

The blood-pressure 7 hours after the injection was usually lower than before. The average of blood-pressure on subsequent days was also usually lower, more markedly in the diastolic than in the systolic pressure. During the injection both pressures were nearly always high. Rolleston (*Brit. Med. Jour.*, Aug. 21, 1915).

The writer found the Almen-Nylander test for glucose in the urine strongly positive in over 50 syphilitics tested during or after arsphenamin treatment. Neither before nor later was there any indication of glycosuria. M. Trossarello (*Riforma Med.*, July 31, 1920).

Intravenous injection of lethal doses of acid nonneutralized solutions of arsphenamin in experimental animals produces widespread and severe vascular injury characterized by congestion, thrombus formation, hemorrhage, and cellular degeneration. The intravenous injection of single large doses

of solutions of disodium arsphenamin (10 times larger than the maximum amount administered to human beings at one time) produces severe vascular and tissue alterations, particularly in the liver, kidney, suprarenals and spleen. The intravenous injection of multiple therapeutic doses corresponding to doses of 0.6 Gm. per 60 kilograms of body weight produces inconspicuous tissue alterations. Kolmer and Lucke (*Arch. of Dermat. and Syph.*, Apr., part 2, 1921).

Blood analyses immediately after intravenous arsphenamin injection showed only 37.9 of the arsenic administered present in the blood; this corresponded to 3.71 mgm. of metallic arsenic per 100 Gm. of dried specimen. J. A. Fordyce, I. Rosen and C. N. Myers (*Amer. Jour. of Syph.*, Jan., 1923).

**Histological Alterations Produced in the Viscera.**—The incidence of these alterations appears to depend, at least in so far as experimental work would indicate, upon two factors: (1) the dose given, and (2) individual susceptibility or idiosyncrasy. The work of Kolmer and Schamberg in animals, to which the doses administered—by mouth—were, in their opinion, about equivalent to those given intravenously to man, seemed to show that in ordinary amounts given to healthy animals, salvarsan does not produce appreciable degenerative changes in the principal organs within a period of four days. With larger though still sublethal doses, however, fatty changes were found by Chirokogorov to have occurred in a certain proportion of the animals experimented upon. The doses used by this author were 0.05 to 0.2 Gm., given subcutaneously or intramuscularly. In 2 of the 4 rabbit experiments of which he gives protocols, the heart showed a mild degree of fatty change and the liver fat glob-

ules decidedly in excess of those normally present in the cells; one of these rabbits also showed abnormal fatty changes in the kidneys. Two dogs weighing about 17 and 20 kilograms and given, respectively, 0.5 and 0.6 Gm. of salvarsan, when sacrificed showed no fatty changes in any of the organs. Pronounced changes in the liver, however, were found in mice given lethal doses. The final conclusion reached by Chirokogorov is that salvarsan undoubtedly does sometimes produce fatty changes, but that the tendency to this varies in different species and also to a wide extent in different individuals of the same species. [The degenerative changes found by Chirokogorov in one of the rabbits are shown in the annexed plate: Fig. 1. Zeiss,  $\frac{1}{2}$  oil immersion, No. 2 eyepiece: Fatty degeneration (red granulations) in heart muscle of a rabbit weighing 800 Gm. and given subcutaneously 0.05 Gm. of salvarsan. Fig. 2. Zeiss, E. objective, No. 4 eyepiece: Fatty degeneration of kidney in same rabbit. Fig. 3. Leitz, No. 3 objective, No. 3 eyepiece: Fatty degeneration of liver in same rabbit. Fig. 4: Zeiss, E objective, No. 3 eyepiece: Muscular lesions at seat of injection, consisting of fatty degeneration, accumulation of leucocytes, and partial hyaline degeneration of the muscles.]

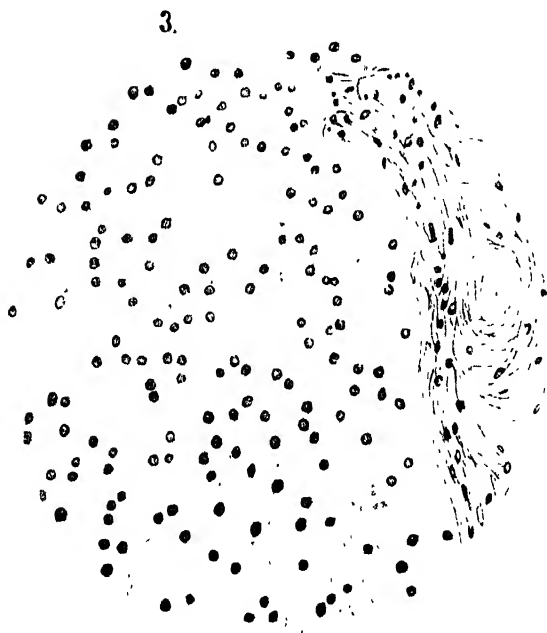
That the variations observed among different individual animals by Chirokogorov hold good likewise in man is suggested by the histological changes seen in certain of the salvarsan fatalities in the human subject. Thus, among 18 cases of death following salvarsan collected by Martius, a few only showed fatty degeneration of the heart, liver, and kidneys. Hofmann

reported the production of subacute yellow atrophy of the liver in a boy 5 years old by two salvarsan injections. Fischer witnessed a case of death from acute encephalitis in which changes were found in the heart muscle, liver, and brain-cells.

**UNTOWARD EFFECTS AND POISONING.**—Toxic symptoms following arsphenamin injections may arise either independently of the drug, *i.e.*, from an improper manner of administration, or because of some direct or indirect effect of the drug itself.

The use in preparation of arsphenamin for intravenous injection of water that has not been redistilled a few hours before very frequently leads to the appearance of headache, fever, rigors, and vomiting, owing to the effects of the toxins from saprophytic bacteria or fungi that have grown in the distilled water in the intervals. Before this fact had been discovered by Wechsellmann the untoward effects following intravenous injection were attributed largely to the salvarsan itself. That old distilled water is actually their cause, however, is proven by the fact that the same symptoms occur when the water is injected alone. Experimental work by Yakimoff has shown clearly, moreover, that simultaneous injection of bacterial endotoxins, such as may occur in distilled water, lowers the lethal dose of the drug as much as three and one-half times. Where saline solution is made from distilled water, experience has shown that it should preferably be boiled again after the salt has been dissolved.

A comprehensive experimental study led the writers to the following conclusions: Single massive doses of arsphenamin, approaching the maximum tolerated dose of



Degenerative Changes Occurring in a Rabbit After the Administration  
of a Non-lethal Dose of Salvarsan. (*Chirokoqorog.*)



the drug for white rats, in rabbits produce severe *nephritis* followed by death. Single large doses of arsphenamin (about one-half of the maximum tolerated dose) cause acute *nephritis*, which generally clears up within from 10 to 16 days. Repeated, normal therapeutic doses of the drug do not disturb the renal functions at all. Whether compared weight for weight or on the basis of arsenic content, neoarsphenamin is more than twice less injurious to the kidneys than arsphenamin. Raiziss and Brown (*Arch. of Derm. and Syphilis*, July, 1924).

Complications due to the arsphenamins are steadily diminishing in spite of the very widespread use of these drugs. In ordinary doses arsphenamin is not toxic, but prolonged circulation of it in the blood, due to delayed elimination because of prior infectious disease or other causes, may result in its conversion into the toxic arsenic oxide. This may injure the epithelium of the capillaries and render these vessels permeable to fluids. Hence the eruptions and central nervous manifestations sometimes witnessed. Simultaneous use of mercury and arsphenamin results in serious impairment of elimination by the former drug, eruptions resulting from the capillary injury thereby engendered. The brain symptoms are due to capillary injury, with subsequent edema, extravasation of red cells and purpura cerebri, wrongly termed *encephalitis hemorrhagica*. The drug has no actual neurotropic action. Wechselmann (*Urol. and Cut. Rev.*, Dec., 1924)

In 2800 patients to whom 27,000 intravenous injections were given, the immediate complications were benign and without consequence. There were 3 cases of erythrodermia, 1 of grave jaundice, 1 of toxic polyneuritis in a tabetic, and 1 case of tardy convulsions with urticaria, all ending in recovery. Death occurred after 1 injection in 1 case; after the fifth injection in another. No satisfactory explanation of the fatal issue can be given. Laurent (*Ann. des Mal. Vénériennes*, Nov., 1925).

Excluding the phenomena already referred to, there may occur in a minority of cases various symptoms due to unusual susceptibility of the patient to arsenic or to toxins set free owing to the action of the drug on the spirochetes or the patient's tissues. Some of these symptoms are identical with those due to old distilled water, viz., headache, malaise, vomiting, and prostration. But there may also be noted pain in the abdomen, diarrhea, jaundice, somnolence, angina, skin eruptions, and in the unusual serious cases, coma due to hemorrhagic encephalitis or involvement of the kidneys and liver. (Hemorrhagic encephalitis has likewise been attributed to old distilled water). Where the drug is given in suitable dosage and with correct technique to individuals that are not unusually susceptible to arsenic, the only symptoms to be expected are slight anorexia and a sensation of physical depression not exceeding a day in duration (Martin).

True toxic effects from neoarsphenamin are neither anaphylactic nor colloidoclastic in nature, but are analogous to the effects of fatal doses in rabbits, featured in particular by general vascular dilatation, serous effusions and exophthalmos. A selective action of the drug on the endocrine-sympathetic system is thereby indicated, and these complications occur where some part of this system is impaired by syphilis or other preëxisting diseases. In Addison's disease and exophthalmic goiter the drug is poorly borne. The chief vasomotor manifestations are mucocutaneous or visceral nitritoid crises, serous apoplexy and vesiculo-edematous erythrodermia. Milian (*Paris méd.*, Mar. 1, 1924).

In the writer's investigation of 317 patients taking arsenicals, nearly all testified to a taste or smell of ether or garlic. It was transient usually, and

his experience indicates that when these sensations persist, it is a sign warning of intolerance of the drug. It seems to be impossible to modify this paresthesia with the usual drugs; **adrenalin** alone reduced it somewhat. Donato (Policlinico, June 29, 1925).

**NITRITOID CRISES.**—Certain toxic symptoms were studied by Milian, who, from their resemblance to the effects of amyl nitrite, calls them "*crises nitritoides*." The onset is very sudden, often during an intravenous injection or soon after. The face becomes flushed, the conjunctivæ injected, the lips and tongue may swell, marked chilliness with rigors occurs, perspiration is profuse, and usually nausea followed by vomiting is noted. Some attacks are accompanied by severe headache, epiphora, and dyspnea, with intense pain in the precordium or epigastrium. Fever and diarrhea are not uncommon. The pulse is usually rapid. A severe attack may end in syncope. Similar, but milder, attacks on the third or fourth day are known as secondary nitritoid crises.

A "serous apoplexy" also due to vasodilatation has been noted after intravenous use of salvarsan and neo-salvarsan. Suddenly, 3 or 4 days after the injection, the patient becomes agitated and develops epileptiform seizures, clonic and tonic, which become more and more frequent. Coma ensues, with death on the fourth day in most cases. At autopsy engorgement of the lateral ventricles and cerebrospinal canal have been noted. Fatal cases of nitritoid crises have shown marked congestion of all the viscera.

Adrenal insufficiency plays the leading rôle in these attacks, which usually respond to adrenalin. **Adrenalin** is given intravenously in the grave cases, especially those of

serous apoplexy. The usual route is the intramuscular, with a minimum dose of 1 c.c. (16 minims) of a 1:1000 solution. In marked cases even 4 c.c. (1 dram) can be given. Beeson (Urologic and Cutan. Rev., Sept., 1915).

Nitritoid attacks are due to vasodilatation, and also to the formation of a precipitate which is arrested temporarily in the capillaries. A sufficiency of alkali with the drug will prevent these effects in persons with normal blood-composition. J. Danysz (Presse méd., Sept. 14, 1916).

At least 3 *explanations of the nitritoid crises* have been advanced, viz., colloidoclastic shock, anaphylaxis, and sympathico-endocrin disturbance. The writers believe these 3 theories to be neither incompatible nor mutually exclusive; the 3 forms of disturbance may be combined in the individual case. Flandin, Tzanck, and Roberti (Bull. et mém. de la Soc. méd. des hôp. de Paris, Nov. 3, 1921).

*Endocrin disturbances* predispose to nitritoid crises. Thyroid changes may occur during treatment. The physician should be on his guard against toxic effects from arsphenamin in cases with irregular menstruation, transient edema, or other vasomotor or endocrin symptoms. Weakness, lassitude in the morning and apathy point toward adrenal insufficiency. Lévy, Juster and Lafont (Ann. des mal. vén., Feb., 1923).

A form of *localized nitritoid crisis* is emphasized from experience with 5 cases of edema of the extremities and moderate cyanosis developing less than 1 hour after arsphenamin injection; 17 other cases receiving the same preparation showed no untoward effect. Bertaccini (Policlin., May 28, 1923).

Every intravenous injection of arsphenamin is followed by a slight decrease of leukocytes in the peripheral vessels of the entire body. It is known that this decrease is influenced by stimulation of the autonomic nervous system and its sympathetic part. Thus, every injection of arsphenamin has a direct influence on the autonomic nervous

system. The angioneurotic symptoms sometimes following arsphenamin are objectively manifest in a marked decrease of leukocytes in the peripheral vessels. **Adrenalin** prevents this decrease of leukocytes. Most persons exhibiting the nitritoid crisis after arsphenamin do not react in this way to silver arsphenamin. Since injections of this drug are generally unattended with any change in the leukocytes, the indication is against any disturbance of the involuntary nervous and vascular systems. Rosen, Müller and Myers (Arch. of Derm. and Syph., Sept. and Nov., 1924).

**Treatment.**—In the case of the early, immediate reactions such as sudden syncope, edema of the lips, tongue or an extremity, severe headache, substernal constriction with dyspnea, abdominal cramps, etc., or of combined phenomena such as follow amyl nitrite inhalation, S. S. Greenbaum (Therap. Gaz., Oct., 1924) finds that subcutaneous or intramuscular injections of  $7\frac{1}{2}$  to 15 minims (0.5 to 1 c.c.) of 1:1000 **adrenalin chloride** with  $\frac{1}{150}$  grain (0.0004 Gm.) of **atropine sulphate** will in most instances decrease or prevent the reaction, provided it is given not less than 15 minutes before the arsenobenzol injection. Flandin's manner of **drawing blood into the arsenobenzol solution** immediately before injection appears of some value. The curative treatment is the same.

**JAUNDICE.**—According to J. F. Schamberg and H. Brown (Jour. Amer. Med. Assoc., June 14, 1924), the organ dominantly attacked by the arsphenamins is the liver. Blood bilirubin determinations by the *van den Bergh quantitative test* will often disclose pathologic amounts of bilirubin before clinical evidences of jaundice are present. By occasional determinations

in patients receiving arsenical therapy liver damage may in some cases be averted. Anything over 2 parts of bilirubin per million of blood is regarded as excessive. In 2 cases referred to it rose to above 150 in the presence of jaundice, then receded to normal as the jaundice passed off. The test appeared valuable in determining when a damaged liver will permit the resumption of treatment. E. Kahn (Münch. med. Woch., Apr. 6, 1923) favors the simple *urobilinogen test* of the urine as a criterion of injury to the liver.

The jaundice, according to Greenbaum, may be either toxic or syphilitic (Jarisch-Herxheimer reaction and hepato-recurrence). Differentiation is not always possible, and is usually based on the amount and regularity of the treatment. The premonitory symptoms—lassitude, malaise, anorexia, chronic headache, insomnia—and the laboratory findings—delayed phenoltetrachlorophthalein elimination and hyperbilirubinemia—indicate an oncoming jaundice of toxic type if observed during a regular series of arsphenamin injections.

In about 40 per cent. of cases hematoporphyrin appears in the urine after injection of salvarsan. Its production seems to depend on an abnormal destruction of hemoglobin with which the liver cannot deal, and which consequently is eliminated by the kidneys. C. Cavina (Giorn. ital. d. mal. ven. e delle pelle, fasc. v, p. 315, 1917).

Report of 2 cases of slowly fatal icterus gravis occurring 1 and 2 weeks, respectively, after a series of 5 doses of novarsenobillon. There was great reduction in the size of the liver, with persistent vomiting, and progressive weakness. Death resulted 21 and 40 days after the onset of symptoms and at necropsy the liver in each case was found in a peculiar condition of cirrhosis with atrophy and acute degener-

ation. Fenwick, Sweet and Lowe (Brit. Med. Jour., Apr. 20, 1918).

The writer has never encountered an instance of toxic jaundice from intramuscular injections of sulpharsphenamin. In a personal case these injections apparently cured syphilitic jaundice. Experiments on rabbits indicated that intramuscular injections of arsphenamin are less toxic for the liver than the intravenous. Their action is the same, although somewhat retarded. Masson (Paris Médical, Nov. 14, 1925).

**Treatment.**—**Duodenal lavage** is recommended by L. F. X. Wilhelm (Arch. of Derm. and Syph., Oct., 1924) on the basis of experience in 33 cases. The stomach is first washed through the tube until the return is clear. The duodenum is then washed with water at 40° C.; 100 c.c. of saturated **magnesium sulphate** solution is then washed back and forth in a 100 c.c. syringe for 10 minutes, after which the duodenal contents are permitted to syphon out. Upon repetition of this procedure 3 or 4 times at ½ hour intervals, the treatment is concluded by washing out the stomach. One to 8 such treatments on alternate days were given, the average required being 2. Other measures employed were: **Acid sodium phosphate**; **oxgall** tablets; **calomel** and a **saline purgative**; **glucose solution proctoclysis** in severe cases; diet rich in carbohydrates and fresh fruits, with restriction of meats. Greenbaum (Therap. Gaz., Oct., 1924) deems the best treatment available to be **biliary drainage** in combination with daily intravenous injections of **thiosinamin** and a diet rich in carbohydrates.

In 28 cases of chronic arsphenamin poisoning treated by the writer, including 16 of jaundice, 11 of dermatitis and 1 of hyperpyrexia, a portion of the cases were treated with a **fat-free diet**,

**forced fluids**, **purgation** and local skin measures, while the others received **intramin** intramuscularly in addition. H. G. Lloyd (Boston Med. and Surg. Jour., Apr. 10, 1924).

**ANEMIA.**—Many cases are met with suffering from profound blood derangement following the use of antisymphilitic remedies, according to L. Stern (Med. Jour. and Rec., Jan. 16, 1924). In such patients he has found valuable intravenous injections of **iron cacodylate** from ampules each containing 1 grain in 5 c.c. An accurately prepared and tested preparation is requisite.

The writer found experimentally that excess of potassium enhances the toxicity of the arsphenamins. An excessive vegetable diet may favor such a toxic action clinically. **Calcium chloride** in 10 per cent. solution in 5 c.c. ampules, given along with the neoarsphenamin, which is dissolved in it, counteracts this form of toxicity, as clinically noted in cases in which, without the calcium, nephritis or eruptions had previously developed. The calcium solution must be injected *slowly* and the drawing of blood into the syringe avoided. Jacobsohn and Sklarz (Klin. Woch., July 8, 1924).

**HEMORRHAGES.**—P. Emile-Weil and Isch-Wall (Presse méd., July 28, 1923), reporting 10 cases of hemorrhage such as epistaxis, hemoptysis, bleeding from the gums, menorrhagia and purpura, warn against persistence in arsphenamin treatment where there is the least hemorrhagic tendency. In mild cases, **injections of human blood** proved effective; in the severe ones, repeated **blood transfusion**, 200 to 300 c.c., was availed of. Other measures comprise **proctoclysis of glucose solution** containing a maceration of 100 Gm. of **hog's liver**, and 40 drops of **adrenalin** solution by the mouth. For resumption of treatment, bismuth



seemed preferable to mercury. There was always intolerance of the arsphenamins in cases with abnormal bleeding time.

Case of death from anemia due to persistent hemorrhages within 2 weeks after 0.6 Gm. of arsphenamin in a hemophiliac was observed by the writer. The drug is contraindicated in hemophilia. J. Rosenbloom (Jour. of Lab. and Clin. Med., Oct., 1923).

**RENAL DISORDERS.**—G. W. Raiziss and H. Brown (Arch. of Derm. and Syph., July, 1924), from experimental work, deem it possible that many of the reactions following the arsphenamins are only secondary manifestations resulting from injuries sustained by the kidneys. In rabbits, 1 large dose of 150 mgm. of neoarsphenamin per kilo. caused acute nephritis, though multiple therapeutic doses of 15 mgm. did not injure the kidneys. Neoarsphenamin, weight for weight or on the basis of arsenic content, proved less than half as injurious to the kidneys as arsphenamin. Clinically, the renal function must be carefully noted before and during the treatment.

Investigations have confirmed the view that more of the drug is eliminated by the intestines than by the kidneys, after intravenous injection. The bile from a dog with a bile fistula constantly showed more than 0.01 Gm. of the drug in 5 c.c. of bile, while 15 c.c. of the urine contained only fractions of a milligram. The amount of bile secreted in 24 hours being about equal to that of the urine, the importance of this route of elimination is plain. The author also refers to Jean-selme's case in which 0.01 Gm. of arsenic was found in the vomitus from 5 to 8 hours after an injection of 0.6 Gm. of arsphenamin. Pomaret (Médecine, Nov., 1920).

Elimination of arsenic by the urine continues for a period of 10 or 12 days.

It is found also in the feces. The maximum excretion occurs on the day of administration or the next day. Each successive injection causes a higher second day rise and higher daily average excretion than the one preceding it. Arsenic is slow in appearing in the intestinal contents, yet the greater part of it is excreted by this route. In the intervals between treatments, the arsenic compounds are retained in the body up to a point of saturation of the tissues. When this point has been reached (apparently about the fourth injection), further additions are in large measure quickly eliminated. Underhill and Davis (Arch. of Derm. and Syph., Jan., 1922).

**SKIN ERUPTIONS.**—The early delayed or intermediate reaction to arsphenamin, developing in 3 to 24 hours, consists, as described by Greenbaum (Therap. Gaz., Oct., 1924), of 1 or all of the following: chilliness, headache, nausea, vomiting, diarrhea, tenderness over the liver, urobilinuria, fever, malaise, *erythematous rash*, and localized or generalized edema. Lowering the dose usually prevents their repetition. Among the late toxic reactions, occurring after 24 hours, is *dermatitis*, frequently preceded by premonitory signs such as localized or generalized pruritus, erythema on the arms and legs, numbness and tingling in the fingers and toes, and hypersensitiveness of the skin (*e.g.*, to tincture of iodine). When the dermatitis occurs early, *i.e.*, after the 1st or 2d injection, these premonitory signs are wanting. Dermatitis persists from a few days to 4 or more months. An apparently mild form may progressively become very severe. All forms are later complicated by secondary infection of the skin, scalp and eyes, as well as by a secondary fever.

Chronic focal and acute prodromal or intercurrent infections form a part of the complex on which arsphenamin

skin reactions develop. Stokes and Cathcart (Arch. of Derm. and Syph., Jan., 1923).

Case of scarlatinoid eruption following the 30th daily injection of arsphenamin. Subsequently, as little as 1 mgm. of the drug sufficed to produce intense anaphylactic shock and eruption. **Sodium bicarbonate** was used with moderate success as preventive. Raynaud, Montpellier and Lacroix (Bull. Soc. méd. des hôp. de Paris, June 22, 1923).

Seborrheic dermatitis seems to predispose to arsphenamin eruptions. H. E. Miller (Cal. State Jour. of Med., Nov., 1923).

Case of grave and persistent melanosis following 11 doses of neoarsphenamin, which closely recalled arsenical melanosis. W. J. O'Donovan (Brit. Jour. of Derm. and Syph., Feb., 1925).

**Treatment.**—**Sodium thiosulphate**, preferably given intravenously, was found by W. L. McBride and C. C. Dennie (Arch. of Derm. and Syph., Jan., 1923) markedly to shorten the course of arsenical dermatitis. It also proved a successful neutralizing agent for acute and chronic mercurial poisoning. When pure, it is non-toxic in doses up to 2 Gm. The treatment is based on the detoxicating, precipitant action of sulphur salts on metals. According to M. R. Groehl and C. N. Myers (Therap. Gaz., Oct., 1924), the drug assists by producing new soluble products of the metals, which are probably thio-sulphuric acid derivatives of a complex protein compound. Intravenous use (0.6 Gm. daily) results in more rapid excretion and a more abortive effect than oral use (30 Gm. daily). A useful preventive measure is to give the arsenical in a dilute solution in 0.4 per cent. **sodium chloride**, allowed to stand 15 to 20 minutes before injection. Dilution in concentrated **lactose** or **glucose solution** (2 to 4 Gm. of the sugar)

is also a preventive measure, but it reduces the therapeutic activity of the arsenical.

**Sodium thiosulphate** was injected intravenously in 3 cases, in doses of 0.3, 0.45, 0.6, 0.9, 1.2, 1.5 and 1.8 Gm. on alternate days, the solution being re-billed before use. Excellent results were obtained. Hoffmann and Schreus (Münch. med. Woch., Dec. 14, 1923).

The writers gave 4 intravenous injections to a total of 1.35 Gm. in a child of 27 months with eczematous and exfoliative dermatitis, the skin lesions almost disappearing in 6 days. Bugg and Folkoff (Bull. Johns Hopk. Hosp., Mar., 1924).

On the basis of Voegtlin's observation that certain sulphydryl (SH) compounds possess detoxifying effects on arsenoxide, the writer used **thiosinamin**, a substitute sulphydryl compound, instead of sodium thiosulphate. It is soluble in 2 parts of water and acts, when given intravenously, extremely rapidly. The drug is used from ampules containing 3 grains (0.2 Gm.) of it in 6 c.c. (96 minims) of distilled water, with 1 or 2 drops of 2 per cent. glycerin added to insure permanent dissolution. The ampules are sterilized in the autoclave. The average daily dose is 1 ampule. The drug yielded excellent results in a large number of cases, seemingly inhibiting the dermatitis almost at once. Greenbaum (Jour. Amer. Med. Assoc., July 5, 1924).

**MISCELLANEOUS UNTO-  
WARD EFFECTS.**—Repeated injections of salvarsan are more likely to cause toxic effects than a single injection, apparently owing to accumulation of the drug or its products in the system.

It has been repeatedly noticed that where other pathogenic micro-organisms than the spirochete are present the toxic effects are more marked than usual. Thus, as stated by McDonagh, an injection of salvarsan in a patient with septic tonsillitis or

influenza will cause an uncommonly pronounced reaction, and may aggravate the disorder present. In the same way, a latent bronchitic process may be excited to renewed activity by salvarsan. Epileptiform seizures have been known to follow the administration of the drug in patients who are particularly predisposed to such disturbances.

Neoarsphenamin in rather large doses by vein passes directly to the liver and is apt to cause injury with resulting jaundice. This subsides if the drug is suspended. Again, the toxic injury of the liver reduces its resisting power, and thus the spirochetes are enabled to settle in it and damage it further. Subcutaneous injection does not reach the liver so directly. L. Brocq (Bull. méd., Mar. 19, 1921).

Reawakening of latent diseases may also occur. A case of latent *malaria* in which the disease was reawakened by novarsenobenzol was reported by the writer.. The arsenobenzols are, however, specific for malaria, which may be cured by simply continuing their use. He thinks many effects attributed to arsenicals are really due to awakened latent infections, such as measles, rubella, lichen planus, or the infectious erythemas. G. Milian (Ann. des mal. vén., Jan., 1922).

*Herxheimer's reaction* consists of a prompt but temporary aggravation or greater prominence of a syphilitic skin eruption present at the time of the injection. The phenomenon is devoid of any unfavorable significance, probably signifying that the drug has caused transient increased activity of the spirochetes, just as, *e.g.*, atoxyl will cause augmented motility of the trypanosomes before they succumb to its toxic action in the sleeping sickness. Where, however, as is sometimes the case, the Herxheimer reaction appears not im-

mediately but a few days after the injection, the cause is probably the toxins set free by the destruction of the spirochetes.

*Morbilliform eruptions*, urticaria, herpes zoster, and angioneurotic edema have also been observed to follow arsphenamin, generally about a week after the injection.

The so-called "*neurorecurrences*" (neurofixation), consisting usually of the appearance in syphilitics of paralysis of one or more of the cranial nerves, especially the auditory and optic, have been fairly definitely shown to be due almost always to the syphilitic process itself, and not, as for a time seemed plausible, to direct or indirect effects of the arsenical drug. This is indicated by the marked improvement which occurs after further treatment by salvarsan or mercury. As McDonagh observes, neuritis of cranial nerves after salvarsan almost always occurs in patients in the early secondary stage of syphilis, the Wassermann reaction being generally negative, and only one injection of the remedy having been given. Apparently the reason for the sudden widespread interest aroused in "*neurorecurrences*" is that the introduction of salvarsan led, in conjunction with the observations of its effects on the disease, to a much closer study of early syphilitic involvement of the cranial nerves and to a realization of the fact that the gradually developing lesions of this kind are far more frequent accompaniments of the disease than had previously been supposed. On the whole, cranial nerve trouble merely implies insufficient treatment. Where series of arsphenamin injections are given, such a condition is rarely seen.

Case of secondary syphilis treated with novarsenobillon, in which 56 hours after the second dose the patient began to vomit. During the next 3 days he had 7 *epileptiform convulsions* with unconsciousness, biting of the tongue, incontinence of urine and feces, a macular skin eruption, marked cyanosis, and failing pulse. Adrenalin, calomel and lumbar puncture failed to relieve, so oxygen inhalations and caffeine, 0.2 Gm. (3 grains), with urotropin, 1.5 Gm. (23 grains), in 15 c.c. (½ ounce) of sterile distilled water, were given. Five hours later the patient had become entirely rational, but he continued to have *partial amnesia* for 14 days. Parnell and Dudley (Lancet, Jan. 24, 1920).

Case of a girl 19 years old, in whom injection of salvarsan was followed by the *phenomena of disease of the basal ganglia*. There was a mask-like facies, with dropping of the lower jaw, delayed execution of various movements in spite of good muscular power, tremor, rigidity on passive motion, horizontal nystagmus, slow monotonous speech, imperfect articulation, and uncertain gait. The blood Wassermann was positive and the spinal fluid Wassermann negative. Paul Matzdorff (Berl. klin. Woch., May 6, 1922).

The writers observed 6 cases of arsphenamin neuritis, 2 simulating incipient tabes and 4 a pseudotabes. Large doses of the drug are an undeniable factor in the neuritis, but it may occur with small doses, probably owing to anaphylaxis. The neuritis seems to be more frequent with subcutaneous injections than with intravenous, since the elimination of arsenic is more rapid with the latter. Persistence of the pupil reflex, integrity of the sphincters, tingling in the soles, and slight changes of sensibility in the limbs are the differential signs from tabes. Sézary and Chabanier (Bull. de la Soc. méd. des hôp., Feb. 20, 1925).

## DEATHS FROM SALVARSAN

have in the great majority of cases occurred either where contraindications have been disregarded; where

the drug has been given as a last resort, with but little hope that it would bring about recovery; or where the technique followed has been faulty or a manifestly excessive dose given. Wechseltmann, at the close of his monograph on salvarsan fatalities, emphasized the fact that these cases present no definite type—except, perhaps, the group of those succumbing to hemorrhagic encephalitis—and can, therefore, not be collectively discussed or explained. He considers renal insufficiency, however, and not abnormal sensitiveness of the brain-centers, the essential condition predisposing to salvarsan death. Accumulation of arsenic in an organism in which the viscera are normal functionally cannot be considered a cause, as Wechseltmann has given doses of 0.6 Gm. ten to fifteen times at intervals of but two or three days without witnessing any ill effects, whereas in many of the fatal cases only 0.3 to 0.8 Gm. had been given altogether. Neither can idiosyncrasy be incriminated, for in many instances death has been produced, not after the first, but after the second or a subsequent injection.

Four deaths following the use of arsphenamin are reported by the writer. From 4 to 6 intravenous doses had been given, with an average interval of 4 days between injections. From 0.4 to 0.6 Gm. of arsphenamin were given at a time. Two days in 3 cases and 3 days in the other case intervened between the time of the last treatment and the onset of the illness. A striking similarity in symptoms as well as in post-mortem findings existed in all 4 cases. After a symptomless latent period of about 2 days, sudden and profound coma predominated, making it difficult to elicit any focalizing signs. There were no cranial nerve palsies; the pupils were dilated

in 2 cases; in two they were unaffected. Two patients had convulsions; Cheyne-Stokes breathing was present in all and death was apparently due to failure of the respiratory center. Pathologic study of the brains of these 4 cases showed similar lesions. These consisted in minute hemorrhages, scattered through and confined to the basal nuclei and that part of the cerebrum bounding the lateral ventricles. These were associated with a softening confined to this locality and seen easiest on gross examination. Cerebral congestion and edema were marked. Blanton (Amer. Jour. of Syphilis, Oct., 1919).

Illustrating possible late fatalities from neoarsphenamin, the writer reports the case of a young man of 23 who had been given in 20 intravenous injections a total of 11 Gm. of neoarsphenamin. Five days after the last injection he developed febrile gastric disturbance and headache, followed by pain in the right side, jaundice, convulsions, hemorrhages, coma, and death on the fifth day. Necropsy showed congestion of all organs, especially the lungs and liver, and disseminated suffusions in the brain. No arsenic was found after careful analysis of a portion of the liver. It is thought possible that the intravenous injections may affect the *endocrin glands* either directly or through the sympathetic system. Van Wimsen (Arch. Méd. Belges, Feb., 1922).

The morbid phenomena witnessed in these cases before death do not correspond with those of arsenic poisoning.

A man of 32, six years after infection, was given an intravenous injection of 0.6 Gm. salvarsan. Symptoms of gastric and brain disturbances appeared on the second and third days, and at necropsy, six days after the injection, the brain showed traces of acute hemorrhagic encephalitis, the blood escaping by diapedesis as in infectious processes. The brain may have been peculiarly sensitive in this patient, as he had had much worry and sought relief from insomnia in dis-

tractions of varied kinds. Almkvist (Munch. med. Woch., Aug. 22, 1911).

Death occurring in hopeless cases—big aortic aneurisms, severe cardiac disease, advanced tuberculosis, or terminal stages of pernicious anemia—cannot be laid at the door of salvarsan. In these cases minimal doses (0.1 Gm.) should be used. Cases which die with symptoms of encephalitis hemorrhagica, on the other hand, are most likely due to edema resulting from too rapid death of the spirochetes. These accidents can be avoided if all syphilitics who show early brain symptoms are treated with very small doses given at intervals. Complete rest after the injection is strictly indicated. Cerebral pressure symptoms then occurring must be relieved by spinal puncture or even by decompression. Salvarsan is relatively harmless—more so than chloroform, for example; 2 to 3 Gm. can be given during a few weeks. P. Ehrlich (Munch. med. Woch., Nov. 21, 1911).

Report of 2 cases of death after salvarsan. The first, observed by Oltramare, was that of an obese man of 48, syphilitic since 15 years, presenting no evidence of renal or cardiac disturbance or of spinal or brain involvement, who succumbed, after a period of coma, three days after an intravenous injection of 0.6 Gm. of salvarsan in alkaline solution. The autopsy showed leptomeningitis, fatty degeneration of the heart, chronic purulent bronchitis, and bronchopneumonic lesions in the lower lobes of the lungs. Caraven brought to the author's notice the case of a young man of 21, without organic lesions of any kind, who died similarly four days after a second injection of 0.6 Gm. of salvarsan, the first having been given a week previously. The autopsy showed marked congestion of the brain and lungs, reddened and soft kidneys, and hemorrhagic foci in the stomach lining. Gaucher (Bull. de l'Acad. de Méd., Nov. 21, 1911).

Case of a man of 30 with severe convulsions developing on the third day after a second injection of sal-

varsan. The convulsions returned at intervals, with unconsciousness, deviation of the eyeballs, clonic and tonic muscular spasms, and abolition of the pupillary reflex. In the intervals the mind was clear and the reflexes normal, but the man complained of intense headache. He died in coma the second day after the onset of the convulsions. The necropsy findings indicated a severe acute action on the central nervous system and kidneys. Assmann (Berl. klin. Woch., Dec. 16, 1912).

Report of the case of a Sepoy, aged 23 years, thin and somewhat anemic, with a secondary rash, mucous patches and general adenitis. Salvarsan 0.5 Gm. ( $7\frac{1}{2}$  grains), was given intravenously. A good deal of vomiting followed. Six days later he was deeply jaundiced; the stools contained bile and the urine traces of bile and albumin. The liver became enlarged and tender, and the pulse regular but weak, with temperature normal. Collapse and death occurred 6 days later. There must have been storage of arsenic in the liver, causing acute fatty degeneration. Three similar cases are on record. Wadia (Brit. Med. Jour., Jan. 6, 1917).

In a patient undergoing mixed treatment with mercury and salvarsan, the second injection of the latter drug gave rise, after 48 hours, to general nervous phenomena ending in death in 24 hours. At autopsy several hemorrhagic foci were found in the brain, one of the size of a plum being in the central nuclei. Dissauer (Deut. med. Woch., Nov. 22, 1917).

A patient received in all 4 injections of 0.6 Gm. (10 grains) of the new salvarsan product manufactured in the United States under German formula. The first 2 injections were without any marked reaction while he had a little vomiting following the third administration. After the fourth dose he had hardly any discomfort and was about the ward in 10 minutes. Four days later he complained of severe abdominal cramps, and vomited frequently. Diarrhea set in

lasting several days, and vomiting persisted until the end. The vomiting was projectile in type with no nausea. He had temporary abdominal tenderness and there was distension of the bladder, necessitating catheterization. Arsenic poisoning was suggested by the vomiting and languor, with signs of nerve degeneration, probably central. The reflexes became slow and weak. Pupils were sluggish and partially dilated. The temperature became subnormal due to exhaustion, while the pulse rate kept fairly strong to the end. About the third day hypostatic congestion of the lungs set in, followed by paralysis of both limbs and almost complete lack of skin sensitivity. There were involuntary bowel passages. He responded very slowly and could hardly use his arms. Unconsciousness and death ensued in 6 days. F. B. McNierney (U. S. Naval Med. Bull., July, 1918).

Wechselmann, collecting accounts of all or nearly all the post-salvarsan fatalities—in adults only—recorded up to the fall of 1912, cites 6 cases occurring after subcutaneous and 15 after intramuscular injection.

Among the much more numerous cases occurring after intravenous injection, Wechselmann lists 25 in which either the injection was given with the patient already *in extremis*, gross errors of technique were made or lesions of various organs existed, accounting for the fatal results, *e.g.*, tuberculosis, syphilitic meningitis, aneurism, sclerotic changes, cancer, etc. Another series of 10 cases comprises those in which the power to excrete the drug was impaired owing to the effects of chronic alcoholism, syphilis, and mercury on the internal organs. Twenty-five more cases were due to the presence of nephritis; in a large proportion of these anuria and uremic phenomena were noted; in

some the renal changes were apparently slight. In both this and the preceding group, combined salvarsan and mercurial treatment had been administered. The remaining—much smaller—groups include the cases neither subjected to combined treatment nor presenting albuminuria, those dying of acute yellow atrophy of the liver (probably quite independently of the salvarsan), and those suffering from severe diseases other than syphilis, and free of the latter.

A pale, slight man, with syphilitic plaques on the tongue, lips, and several enlarged glands, was ordered biniodide of mercury injections, which were badly borne, and subsequently injections of 40 per cent. gray oil. A year later the glands of the neck were found much enlarged and plaques in the mouth evident. Weight 43 kilos (94 pounds). No albuminuria. No lesion in the heart or lungs. Three hours after an intravenous injection of 0.4 Gm. of salvarsan in alkaline solution, vomiting, diarrhea, and sweats supervened. The vomited matter was greenish and at times mixed with dark blood, the diarrhea abundant and frequent, perspiration copious, and palpitation violent. The lips were violet, the tongue chocolate and dry, the aspect very pale, temperature 36° C. (96.8° F.), radial pulse almost imperceptible. On the two days following the injection, until he died, the patient did not pass a single drop of urine, and the bladder was entirely empty. E. L. Morata (*Rev. de med. y cir. pract.*, Feb. 28, 1911).

A patient received 0.5 Gm. (7½ grains) of salvarsan by vein and after the injection complained of severe abdominal pain. For three days she voided no urine; on the fourth, however, she passed three ounces of clear urine; from then until death on the following day she passed no more. She died in coma. On microscopic examination of the liver the

parenchyma cells in the central part of the lobules were quite irregular in size and shape and had ragged, indistinct margins. Many contained a bright-yellow pigment and all showed vacuoles. The protoplasm was granular and the nuclei of different sizes and shapes, some scarcely distinguishable. Some of the cells contained three or more nuclei, suggesting direct division. Some cells showed mitotic figures in various stages. In the kidneys proliferation of the epithelium was present in all parts of the convoluted tubules. Polynuclear cells were common. Occasionally syncytial, budlike masses of protoplasm were found. There was an excessive amount of desquamation of the epithelial cells. There were no evidences of severe vascular injury, such as is common after arsenical poisoning. H. O. Ruh (*Cleveland Med. Jour.*, Sept., 1912).

Two fatal cases observed following salvarsan. The first was a man, 30 years of age, who received three intravenous injections of 0.6 Gm. each within a period of two months. The first two injections were given two days apart. He also received an injection of metallic mercury. Within a few hours after the third injection of salvarsan there was a slight tingeing of the scleræ and on the following day universal icterus, terminating fatally after four weeks, with the picture of an acute yellow atrophy of the liver. Chemical examination of the liver and spleen gave a definite arsenical mirror.

The second case occurred in a woman of 29 years who had received mercury injections repeatedly. Within two months she received four injections of salvarsan—two intravenously and two intragluteally—the combined dosage being 1.95 Gm. About seven months after the last injection of salvarsan icterus set in, which ended fatally within eighteen days, with the picture of acute yellow atrophy and ascites. Only faint traces of arsenic could be detected in the liver. The pathologicoanatomical

diagnosis was chronic yellow atrophy of the liver. In the second case the condition did not follow soon after the salvarsan was injected, and the concurrence of syphilis as a cause could not be ruled out. Severin and Heinrichsdorff (*Zeit. f. klin. Med.*, Bd lxxvi, 1912).

While recognizing the frequency of brain symptoms in cases of death after salvarsan, Wechselmann, as the result of his comprehensive study, felt impelled to lay most stress upon failure of elimination as the cause of these symptoms. Although the fact that salvarsan may be well borne even by seriously diseased kidneys, but may cause death where the histological changes are slight, would seem to be in opposition to the above view, the work of Schlayer has shown that disturbances of renal function in general by no means necessarily parallel the actual, evident pathological changes present. Moreover, Wechselmann pointed out that arsenic has been demonstrated to impair, even after small doses, the ability of the renal vessels to dilate or contract—thereby tending to arrest the kidney function—while mercury induces essentially a tubular nephritis, with albuminuria and casts. Since nearly all the cases of salvarsan death in robust individuals have shown the combination of energetic mercurial treatment with intravenous administration of the arsenical remedy, Wechselmann was inclined to consider this association responsible for a number of the deaths from salvarsan recorded. That such is actually the case is indicated by a rather extensive array of experimental and clinical evidence, which makes it seem probable that in persons whose kidneys are unusually susceptible to the effects of mercury,

and are therefore somewhat disturbed in function even by ordinary mercurial treatment, the added paralyzing influence of the arsenic in salvarsan on the renal vessels will be sufficient to arrest the renal function. This, in turn, will cause retention of the salvarsan in the system for an unusual period, and a considerable amount of it will become oxidized, forming a compound far more toxic than salvarsan. (Ehrlich himself agreed with Wechselmann that this oxidation in the system may be increased owing to stasis brought on by kidney insufficiency.) Finally, since several observers have noted that salvarsan exposed to the air was particularly likely to bring on anuria, the readiness with which death may occur through the mechanism advanced by Wechselmann will without difficulty be realized.

Comparison between the effects of toxic doses of salvarsan and of bichloride of mercury. Salvarsan has a relatively slight effect upon the kidney and a relatively marked effect upon the liver; about three times as much arsenic will lodge in the hepatic cells as will be found in the renal epithelium. As is well known, bichloride of mercury attacks the kidney with great avidity, so that the organ is rapidly damaged; on the contrary, its action upon the liver is relatively slow and slight, the action in each case bearing a direct relationship to the amount of the drug. Oettinger and Fiessinger, examining a case of poisoning by intramuscular injection of mercury, discovered 0.01 Gm. of mercury for each 1000 Gm. of liver tissue, while three times as much was found in the kidneys. Morel, Mouriquand. and Policard (*Jour. de phys. et path.*, July 15, 1912).

Case of a woman with ulcerative syphilitic lesions of the throat and



labia, previously treated with mercurial inunctions. Urine clear and free of albumin; specific gravity 1014. The ulcers recurring, an injection of 0.6 Gm. of neosalvarsan was given, which was well borne. Eight days later another injection of the same dose was given. Two days after, a slight tremor appeared and the kneejerks became exaggerated. Next day, convulsions, unconsciousness, and cyanosis; followed, a day later, by coma, marked cyanosis, and death. The autopsy revealed a cloudy condition of the epithelium of the convoluted tubules. The cells of Bowman's capsule surrounding the glomeruli were in part thickened, swollen, and detached. Busse-Merian (Münch. med. Woch., No. 43, 1912).

Case of syphilis in the secondary stage in which seven injections of calomel had been given, stomatitis appearing after the fifth. Some albumin in the urine was also noticed. Nine days after the last mercurial injection 0.5 Gm. of neosalvarsan was given intravenously, two days later 0.9 Gm., and in two days more 1.08 Gm. At least seven hours later a mild febrile reaction was noted—38.5° C. (101.3° F.). Next morning the temperature was normal, but some general depression experienced. In the afternoon convulsions and unconsciousness supervened. Venesection and intravenous saline infusion brought about some improvement, but next morning the convulsions recurred and the patient became cyanosed.

Death took place notwithstanding the use of artificial respiration. The post-mortem examination showed thrombosis of the left ulnar vein; embolism of the pulmonary artery; marked parenchymatous degeneration of the renal epithelia in the convoluted tubules, with advanced nuclear necrosis. There were no perceptible changes in the brain. The author considers the case one of retention intoxication due to renal insufficiency. Gennerich (Praxis der Salvarsanbehandlung, p. 20, 1912).

The retention of salvarsan in the blood destroys the oxygen-carrying property of the latter, and deaths after the use of the drug are the result of a severe kidney lesion. Therefore, every salvarsan injection demands the minutest control of the kidney function. Antoni (Deut. med. Woch., March 13, 1913).

Unsuspected abnormal conditions of the heart have been held responsible for death after salvarsan. Thus, Martius reports 7 cases of death by heart-failure occurring at a varying interval after the administration of salvarsan, although symptoms and physical signs of cardiovascular disease had been either absent or present only in slight degree. At autopsy 5 of these cases presented syphilitic aortitis, coronary sclerosis, and myocarditis, and 1 a hypoplasia of the heart and aorta. Wechselmann pointed out, however, that salvarsan does not in itself seem to be injurious to the heart (this has been clearly established in regard to the normal heart) and that in patients suffering from cardiac disease, especially in arteriosclerotics, it is, as a rule, very well borne, generally even improving syphilitic hearts. In cases like those reported by Martius, as well as in instances of cardiac or renal hypoplasia in general, he considers the risk of salvarsan injections to reside at least in part in the accompanying diminished capacity of elimination. The same probably applies to the use of salvarsan in cases suffering from febrile affections.

Guinea-pigs were injected with "606" in doses ranging from 0.009 to 0.12 Gm. per 100 Gm. of body weight and succumbed in one to thirteen days. In those that died in twenty-four hours (dose 0.01 to 0.012) the organs were intensely congested and

contained hemorrhagic foci. The liver was enlarged, the blood-vessels engorged, the trabeculae were compressed, and the hepatic cells around the portal radicles were infiltrated with fat; the kidneys were congested, especially in the cortex; interstitial and intralobular hemorrhages and a small cortical infarct were also observed. The spleen was greatly congested; the Malpighian corpuscles were hypertrophied and infiltrated; the large white cells were increased and filled with blood-pigment. The suprarenal glands showed medullary engorgement. The myocardium was congested. The lungs presented basal congestion and subpleural lobular hemorrhages. The intestines were filled with diarrheal material. In the animals that died on the fourth day, similar changes were found. Those that lived nine to thirteen days were affected to a slighter degree. Gaucher (Bull. de l'Acad. de Méd., Nov. 15, 1910).

A man had well-compensated mild aortic insufficiency, but no other pathological findings were detected in the heart. A few days after subcutaneous injection of 0.3 Gm. salvarsan, signs of heart weakness appeared, proving fatal on the eleventh day. Necropsy revealed unsuspected degeneration of the myocardium, which had evidently been aggravated. Spiethoff (Münch. med. Woch., Jan. 24, 1911).

**Local Untoward Effects.**—Intramuscular injections of salvarsan in some instances cripple the patient for a number of days. An indurated mass may be produced which remains for months, and even, in rare instances, local softening and evacuation of sterile pus may take place. Intense pain may be present for as long as a week. The swelling, which begins about the third day, generally does not *per se* give rise to pain, and subsides, for the most part, at the expiration of a week, only to be

replaced, in many instances, by the induration already referred to. Heat and cold may be alternately applied to relieve any discomfort present, or, if the skin area becomes hyperemic, lead water and laudanum may be used. Fluctuation does not indicate incision, but at most aspiration, as the fluid present is sterile.

Abscesses after intramuscular injection result from one of three causes: improper preparation of the solution or suspension employed, insufficiently deep injection of the drug, and bacterial contamination. Examination of the walls of one of the cavities showed an increase of fibrous tissue, with complete blocking of the smaller vessels and lymphatics by minute particles of salvarsan. Numerous small masses of the substance were also found in pocket-like cavities distributed through the section. There were degenerative changes, with decrease in amount of both connective and elastic tissue. Sutton (Boston Med. and Surg. Jour., Dec. 21, 1911).

Occasional instances of nerve injury due to faulty technique in intravenous arsphenamin injections have been reported. If the injection is made into or near a nerve sheath the nerve will be damaged and sloughing of tissues may occur to such an extent as materially to interfere with the repair of the injured nerves.

The writer observed 2 cases of such injury involving the median and ulnar nerves.

Pain radiating into the fingers during the injection is a warning that the solution is not being injected into the vein. D. Lewis (Jour. Amer. Med. Assoc., June 18, 1921).

Extensive necrosis occurs only after subcutaneous injection. The tissues become transformed into a brownish mass, surrounded by a fibrous capsule. Such necrosis may be avoided by injecting the salvarsan

at several points rather than in one locality alone. It occurs oftener if the drug is administered in the thoracic region than in the gluteal (McDonagh).

Case of thrombosis after intravenous infusion of salvarsan. By accident, the injection was made elsewhere than in the area sterilized for it. The patient was a young man who had had veins punctured for the Wassermann test five times and also for a second infusion of salvarsan, without mishap. The thrombosed vein was resected a month after the infusion, and the *Streptococcus albus* was cultivated from it. Hausmann (Münch. med. Woch., Dec. 13, 1910).

Local reaction after the intravenous method means one or several of the following: (1) Infection. (2) Injection of the fluid into the circumvascular cellular tissue. (3) Penetration and injection of the wall of the vein. (4) Transfixion of the vein and injection into the sublying tissues. (5) Too rapid injection. G. F. Lydston (N. Y. Med. Jour., Oct. 21, 1911).

**Untoward Effects from Neosalvarsan.**—Experience with the newer form of the Ehrlich-Hata remedy seems to have shown that it is in many respects less likely to produce untoward results than the older compound, provided certain contraindications and details of technique be borne in mind, and the injections not given at unduly short intervals. Thus, Bayet states that fever, nausea, vomiting, headache, and general lassitude are less often observed with the new remedy. Stühmer calls attention to the fact that intestinal disturbances and collapse are almost never witnessed with it, although drug rashes are more frequent. Kerl and Schreiber confirm these observations. Rytina found, upon giving intramuscular in-

jections of neosalvarsan, that evidences of a general reaction were limited to a few, in which there was a slight transient nausea and a rise of the temperature up to 99.4° F. McIntosh and Fildes saw no immediate symptoms except diarrhea, though what they term a "spirochete fever," occurring in occasional cases several hours after the intravenous injection, was associated with nausea and vomiting. This fever they do not regard as an expression of the toxicity of the drug, but rather as a syphilitic anaphylactic phenomenon. Schreiber notes that the exanthemata sometimes following full doses of neosalvarsan occur between the eighth and the twelfth day.

The authors have seen no symptoms follow the injection of 1.5 Gm. of neosalvarsan excepting diarrhea in some cases, unassociated with malaise. Nausea or vomiting apart from such occurring with the "spirochete fever" was absent. McIntosh, Fildes, and Parker (Lancet, July 13, 1912).

In a syphilitic woman, aged 31, the phenomena appeared after the fourth injection of the third series. Death occurred 2 months after the last injection. Necropsy revealed extensive ulcerative colitis with perforations and purulent peritonitis, undoubtedly the result of toxic action from the arsenical. Bonnet (Jour. de méd. de Lyon, May 20, 1925).

A few observers appear to have dissented from the view that neosalvarsan is less often followed by toxic effects than salvarsan. Wolff and Mulzer concluded that it is much more poisonous, having observed headache, vomiting, and diarrhea in 14 cases out of 30, a chill in 1 case, extensive eruptions in 4, herpes labialis in 2, and nephritis, paralysis, and other serious phenomena in 1. Kall

neosalvarsan, considerably detoxicated by the introduction of the metal. It is produced by the interaction under certain conditions of neosalvarsan and silver salvarsan. In aqueous solution it does not become more toxic after standing a long time in the air. Its solubility is almost as good as that of neosalvarsan, and it is stated to be as well borne and to have a stronger spirocheticidal action. K. Ullmann (Wiener klin. Woch., Apr. 6, 1922) concluded from over 2 years of experience with silver salvarsan and neosilver salvarsan that both are excellent specifics against syphilis in all its stages. He found them much superior to the earlier salvarsan preparations as regards local tissue reaction. Fabry and Wolff (Med. Klin., Jan. 26, 1922) treated over 100 cases with pure neosilver salvarsan in doses of 0.2 Gm., increased gradually to 0.3 and 0.5 Gm. The preparation was well borne. The effect on the visible symptoms of syphilis was good and in all cases the serum reaction was rendered negative. The writers had hopes of overcoming salvarsan dermatitis by combined treatment with different salvarsan compounds.

**Sulpharsphenamin (Sulpharsenol).**—The therapeutic results from the use of the older arsphenamins and silver arsphenamin in **neurosyphilis** leaving much to be desired, it has been concluded that these compounds fail owing to an insufficient penetrating power, which leaves some of the parasites unkilld, with resulting relapse after cessation of treatment. To overcome this deficiency, other compounds—in particular, sulpharsphenamin and tryparsamide—have been tried as agents possessed of greater penetrating power.

Sulpharsphenamin, in which both amino radicals of arsphenamin are stated to be replaced by methylenesulphonic acid groups, was first used experimentally and clinically in 1919 by Lévy-Bing, Lehnhoff-Wyld and Gerbay under the French designation sulfarsenol. In a 30 to 40 per cent. solution (0.4 Gm. in 1.2 to 1.5 c.c. of distilled water), this drug can be injected *subcutaneously* or *intramuscularly* without excessive irritation. According to C. Voegtlin, J. M. Johnson and H. Dyer (Pub. Health Rep., Nov. 10, 1922), the drug is more stable than neoarsphenamin, both in powder and solution; is of much lower toxicity; is eliminated as rapidly by intra-

muscular as by intravenous injections, and possesses greater ultimate sterilizing power than neoarsphenamin. The same observers, with J. W. Thompson (*Ibid.*, May 11, 1923), showed experimentally that penetration of the nervous system by the drug, given intravenously, is greater than in the case of the older arsenicals, and is comparable to that secured with tryparsamide, claimed the most penetrating arsenical yet devised.

Among the subsequent clinical reports was that of D. L. Belding (Arch. of Derm. and Syph., Apr., 1924), who found the drug as effective as neoarsphenamin in healing syphilitic lesions, but more apt to produce toxic disturbances, especially upon intravenous use of over 0.7 Gm. a week in a 68 kg. patient. Dermatitis occurred in 16 per cent. of 63 patients, and varying degrees of peripheral neuritis, in no case pronounced, in 56 per cent. of 44 adult patients receiving intravenous injections. In the intravenous cases neuritis occurred only when the dose exceeded  $\frac{3}{4}$  the maximum standard for neoarsphenamin. Local reactions occurred oftenest when doses exceeding 0.3 Gm. were injected. The drug is well suited for intramuscular use in adipose women and children.

J. H. Stokes and C. W. Behn (Jour. Amer. Med. Assoc., July 26, 1924) dissent from Belding's conclusions as to the frequent toxic effects from sulpharsphenamin, having used a different preparation. They reported on 126 patients with all types of syphilis who received *intramuscularly* 1360 injections of 0.3 to 0.6 Gm. With the epifascial technique they found sulpharsphenamin of the brand they used could be injected without significant reaction and with no more discomfort than the ordinary mercurial injection. Doses over 0.4 Gm. should be divided between the 2 buttocks. Subcutaneous injection is therapeutically less effective. A 30 to 40 per cent. solution was used, and stress is laid on complete emptying of the 2 c.c. syringe by having a small bubble of air above the injection fluid to clear the needle. Three per cent. of toxic reactions were obtained, 2 patients having fever and 2, exfoliative dermatitis. Therapeutically, sulpharsphenamin intramuscularly proved quite as effective as arsphenamin and neoarsphenamin as to spirillicidal action and effect on the blood Wassermann

and spinal fluid reactions, the healing of lesions, and general well-being. The compound appeared distinctly superior to the older drugs in neurosyphilis and superior to neoarsphenamin intravenously in all aspects of syphilis. It is well borne by patients with cardiovascular disorders, if used in moderate dosage.

Sulpharsenol is deemed nearly ideal for employment in *children* by G. Ahman (Hygiea, Aug. 15, 1924). Subcutaneous injection in a 6 per cent. solution is preferred. In cases in which arsphenamin had not given entirely satisfactory results, the newer drug proved its efficacy.

Taking the chemotherapeutic index (*i.e.*, the maximum tolerated dose over the minimum effective dose) as the criterion of therapeutic efficiency, G. W. Raiziss, M. Severac and J. Moetsch (Jour. Amer. Med. Assoc., Nov. 29, 1924) found that sulpharsphenamin, on the basis of tests in rats infected with *Trypanosoma equiperdum*, is considerably inferior to arsphenamin and at most  $\frac{1}{2}$  as efficient as neoarsphenamin. Its efficiency was practically the same whether given intramuscularly or by vein.

A new arsenical must, according to Fox (Am. Jour. of Syph., July, 1925), fulfil at least one of four requirements to be awarded a real place in the treatment of syphilis: a therapeutic value, in the tolerated dose, superior to that possessed by the older arsphenamins in the attempted cure of the disease; a particular quality in arresting and healing certain of the later manifestations of the disease resistant to other forms of treatment; a decided usefulness in those cases unable to receive arsenic in the older forms because of toxic reaction of one kind or another; superior availability because of simplification of administration by other than the intravenous method, without, of course, loss of therapeutic value or increase of toxicity.

The fourth requirement, then, remains the only one in which the drug possesses any important advantage over the other arsphenamins. Because of the higher incidence of systemic reactions following the use of sulpharsphenamin it seems desirable to confine its employment solely to those cases in which intravenous therapy cannot be used.

**Tryparsamide.**—This compound, chemically *n*-phenylglycine-amide-*p*-arsonic acid,

was synthesized by Jacobs and Heidelberg at the Rockefeller Institute. Its arsenic content is 25.32 per cent. Its main features are given by W. H. Brown and L. Pearce (Jour. Amer. Med. Assoc., Jan. 5, 1924) thus: A moderate degree of trypanocidal action and slight but definite spirocheticidal action; an unusually high penetrability which enables it to develop a high actual as compared with its potential parasiticidal action, and a remarkable power of reinforcing processes of natural resistance and promoting recuperation.

Recording 1 year's experience with it in **paretics** in the Philadelphia General Hospital, F. G. Ebaugh and R. W. Dickson (Jour. Amer. Med. Assoc., Sept. 13, 1924) reported encouraging results in 52 cases. The drug was given intravenously in weekly doses of 3 Gm. (in solution in 10 c.c. sterile distilled water) over a period of 10 weeks. Eight weeks' rest was given after each course of 10 injections. Careful preliminary eye studies were made in each case, and optic atrophy of any degree was ruled out. Of 36 cases in a state of "organic psychosis with functional coloring," 10 were so improved as to be discharged and return to work. In 5 with "transitory psychosis," all were similarly improved. This compared with only 5 cases discharged from the same ward in 1922. The drug frequently gave good results in spite of only meager and transitory serologic improvement. There was marked improvement in the physical condition of all cases, with increased hematopoiesis. One case developed optic atrophy following the first course of tryparsamide. Two had neurorelapses, which responded to further treatment. The writers regard the drug as the best so far advanced for general paralysis.

Similar conclusions were reached by J. E. Moore, H. M. Robinson and R. S. Lyman (Jour. Amer. Med. Assoc., Sept. 20, 1924), who regard the drug as of particular value in early general paralysis, meningovascular neurosyphilis, and the majority of cases of tabes. In primary and secondary syphilis, and in tertiary syphilis without nervous involvement, its therapeutic effect is so slight as to preclude its use. (Even repeated doses of 7 Gm. failed in primary and secondary cases). In early neurosyphilis, the comparatively feeble spirocheticidal value of

tryparsamide precludes its use unless in combination with an arsphenamin. Visual disturbances occurred in 17.8 per cent. of 241 cases, but in only 2.8 per cent. was there noteworthy permanent visual injury. This untoward effect may be largely obviated by ophthalmologic control of treatment, yet should restrict the use of the drug to neurosyphilis and trypanosomiasis. Before treatment, the visual acuity, fundi and visual fields should be carefully examined in each case. Reexamination must be carried out at the first appearance of subjective visual disturbance. At this point, objective injury, if present, is usually so slight as to leave useful vision if the drug is permanently withdrawn.

Further experiences with tryparsamide were reported by H. C. Solomon and H. R. Viets (Jour. Amer. Med. Assoc., Sept. 20, 1924) who treated about 100 cases of neurosyphilis. The conclusion reached was that in some instances the drug gives results better than are obtainable with the older methods, but in other cases does not give as good results. One effect on the spinal fluid was very striking, the cell count being nearly always reduced to normal after 6 or 8 injections. Globulin and total protein were somewhat reduced in many cases. The other spinal fluid findings were not more improved than by other methods. In tabes the results were, on the whole, good, though not as favorable as with the elaborate intraspinal treatment. Four cases in the series developed considerable amblyopia, in 3 of which a permanent defect remained.

According to W. I. Lillie (Jour. Amer. Med. Assoc., Sept. 13, 1924), ocular changes occur as often after arsphenamin as after tryparsamide. The arsenicals appear efficient in decreasing ocular changes in central nervous syphilis. Neff (Wisconsin Med. Jour., Aug., 1925), in the treatment of 15 cases of optic nerve disorder obtained excellent results. Four patients complained of subjective eye symptoms. Immediately on the development of eye symptoms the treatment was discontinued and was only resumed when these had disappeared, or when ophthalmologic examinations justified continuation. On resumption of treatment there was never a recurrence of visual disturbance.

As regards the spinal tract, Fordyce and

Myers (Am. Jour. Med. Sci., July, 1925) found in their examinations of the spinal fluids of patients receiving injections of tryparsamide that in this group arsenic was absent in 14 per cent., the amounts did not exceed those found after other methods of administration. In order to obtain these results, it is necessary to introduce  $7\frac{1}{2}$  times as much drug as in other cases. Briefly, the dosage is extremely large as compared with other drugs. Due to the rapid excretion of tryparsamide, the amount of arsenic available for penetration is extremely small after the 24-hour period. Experimentally, examination of the brain shows that 9 times the arsenic concentration is maintained in the brain after silver arsphenamin with the use of  $\frac{1}{15}$  the amount of arsenic injected. It is shown that tryparsamide does not possess an unusual power of arsenic penetration into the central nervous system.

#### **Pooled Arsphenaminized Fortified Serum.**

—In this procedure, as described by J. G. Marthens (Amer. Jour. of Syph., Apr., 1924), the serums from 20 to 25 patients receiving intensive intravenous treatment are poured into a common beaker and thoroughly mixed. The serum from each is prepared by withdrawing 45 to 60 c.c. of blood  $\frac{1}{2}$  hour after the arsphenamin injection into dry sterile 15 c.c. centrifuge tubes, keeping in the ice-box for several hours, and then centrifuging for 10 minutes, or until all the erythrocytes are excluded. The pooled serum is inactivated on a water bath, and 1 hour before use is "fortified" by addition of 0.5 to 1 c.c. of a solution made by adding 0.5 Gm. of old salvarsan to 150 c.c. of warm, sterile distilled water, alkalinizing with sodium hydroxide, and diluting 10 c.c. to 35 c.c. with 0.5 per cent. saline solution. After this addition to the serum, inactivation for 20 minutes is carried out. Upon receiving the injection of fortified serum intraspinally in **paresis**, for which the fortified serum was created, the patient remains in bed for 48 hours. The intraspinal injection is preceded by an intravenous injection given the day before. The first course of treatment comprises 16 weekly intravenous neoarsphenamin injections and 10 intraspinal injections of the fortified serum at longer intervals. Next mercury inunctions are given daily for a month, with potassium iodide by the

mouth. This is followed by 3 months of rest, next a course of 6 intravenous injections followed by mercury rubs, when the iodide is given again and repeated every 3 months.

### THERAPEUTICS.—In Syphilis.—

As the treatment of syphilis by arsenicals is considered in full under the heading of SYPHILIS in the eighth volume, a summary review of this subject will alone be submitted in the present connection.

The effect of salvarsan in syphilis is considered to be, at least in major part, a direct one upon the causative spirochetes. The remedy is intended to combine with the protoplasm of the parasites and kill the latter without affecting the cells of the host. McIntosh and Fildes have shown, in experimental work on rabbits, that the drug possesses spirocheticidal power far in excess of that of mercury.

Arsphenamin, if used too early in the course of the disease, before it has had a chance to evolve itself completely and stimulate proper resistance, leads to a dangerous situation, in which the patient is not cured of his syphilis and has a focus of infection left with no resistance developed to withstand it. This observer deems arsphenamin dangerous in the early stage of syphilis unless it can be used to the point of eradication; otherwise, it had better be omitted, at least for the first 3 months.

**Mercury** seems to stimulate immunity, and should therefore be used in the early course of the disease. W. A. Pusey (Atlantic Med. Jour., Jan., 1925).

McDonagh refers to the fact that if scrapings from a chancre which is healing under salvarsan are examined before the spirochetes have entirely disappeared, the organisms will be found "swollen, broken up, and not so much curved, but with a swelling somewhere along their course,"—this

swelling probably being analogous to a spore.

The minimal concentration of chemicals required to kill *Treponema pallidum* of a heavy type was, of mercury bichloride, 1 to 200,000; arsenic trioxide, 1 to 30,000; tricoresol, 1 to 500; salvarsan, 1 to 1000; neosalvarsan, about the same as salvarsan. Minute quantities of the antiseptics, far below the sterilizing point, were found to stimulate markedly the growth of spirochetes. The toxic effects of salvarsan were found to be increased from two to five times in the presence of liver and especially blood enzymes. J. Bronfenbrenner and H. Noguchi (Jour. of Pharmacol. and Exper. Therap., March, 1913).

Pharmacological and clinical evidence shows salvarsan kills all the spirochetes it can reach, while mercury promotes the immunity reactions by increasing the protective substances in the recipient. Schreiber (Munch. med. Woch., lxi, 522, 1914).

Studying the influence of salvarsan on immunity in infected animals the author concluded that the destruction of the parasites causes the formation of antibodies which take part in the final sterilization of the organism and produce a temporary immunity. The latter lasts but 4 to 15 days, and is not transmitted from mother to offspring, either directly or through the milk. F. V. Verbitsky (Roussky Vratch, May 9, 1915).

In a series of experiments in rabbits with syphilitic lesions, the writer tried to ascertain the ability of treponemata to accustom themselves to the action of arsenic by injecting minute doses of arsphenamin. After a given period he transplanted the organism from these rabbits to others, which in turn were treated with slightly larger doses of the drug; repeating this procedure until the active therapeutic dose was reached. He succeeded in increasing the resistance to arsenicals in certain strains of treponemata within certain limits. J. V. Klauder (Arch. of Derm. and Syph., Apr., 1924).

The destruction of the spirochetes takes place rapidly under salvarsan; in a few hours they disappear from the primary lesion or papules.

In addition to its parasitocidal effect, salvarsan appears to improve directly the general nutrition of the body, after the manner of small doses of inorganic arsenic.

**Effect on the Wassermann Reaction.**—Salvarsan changes a positive Wassermann reaction into a negative one with greater ease than mercury. Upon repeated injections of the drug, a negative reaction will generally be noted in a month to six weeks, especially in early cases. The more efficient and prompt the antisyphilitic treatment, whether arsenical or mercurial, has been, the sooner will the positive reaction disappear. The latter event is by no means, however, to be construed as an indication to stop treatment, for the negative Wassermann does not show that the disease has already been eradicated, but only that it has been changed from an active state to one of inactivity for the time being.

In controlling the treatment by the Wassermann reaction it must be borne in mind that from 10 to 15 per cent. of the active late manifestations of syphilis give a negative reaction, so that, in the face of positive clinical findings and a negative test, the latter may be disregarded in the late stages of the disease. The author has on several occasions administered salvarsan to patients with a negative Wassermann with the very best results. In 1 case with a marked onychia involving the nails of the hands and feet, a decided change took place after the second injection. John A. Fordyce (Jour. Amer. Med. Assoc., Oct. 5, 1912).

The titration method, when properly controlled, is an accurate and delicate

means of recording the serologic results of treatment. In persons with old untreated syphilis, appreciable fluctuations in the Wassermann reaction, as a rule, do not occur over a period of a few months, although during the active stages of the disease "flare-ups" may take place from time to time. Belding and Holmes (Archives of Dermatology and Syphilology, April, 1924).

In cases where the reaction has been negative for some time a "*provocative*" injection of salvarsan will nearly always cause a return of the positive reaction in cases where the disease has not been definitely removed. This change takes place usually very promptly, the degree of reaction being generally most marked within twenty-four hours after the injection. It does not persist long, however, nearly disappearing by the fifth day in most instances (Gennerich, McDonagh). In the opinion of many observers these provocative injections constitute the most reliable means at hand to determine just when syphilis has been overcome and treatment is no longer necessary. According to Gennerich, however, the negative result of such a test is not to be absolutely accepted as proof of the eradication of the disease until at least eight months have elapsed since treatment has been discontinued.

**Indications for Arsphenamin Treatment in Acquired Syphilis.**—Though at first brought out by Ehrlich as an independently curative remedy for syphilis, the drug has, on the whole, proven itself more valuable for combined treatment with mercury.

The writer makes it a routine practice to examine chancres for the *Spirocheta pallida* both by dark ground illumination and by the India ink method. As soon as the diagnosis is made 0.4



Gm. of arsphenamin is administered. On the following day 1 grain (0.065 Gm.) of metallic mercury in cream, 5 minims (0.3 c.c.) is injected into the gluteal region. The patients get 4 weekly doses of arsphenamin of 0.4 Gm. or 5 weekly doses of 0.3 Gm., followed by an injection of mercurial cream the next day. The mercurial injections are kept up for another 5 weeks, making a total of 9 injections. Neoarsphenamin or galyl may be substituted, in concentrated solution, with 10 c.c. (2½ drams) of freshly distilled water. The primary cases, almost without exception, gave a negative Wassermann reaction after 2 months and remained so in the second test at the end of another 2 months. The secondary cases showed a higher percentage of negative results after the first and second tests, but many of the tertiary cases were positive after the first and second test, showing that it is seldom that a positive reaction, in a case of tertiary syphilis, is converted into a negative after a course of treatment. French (Pract., May, 1916).

No superiority was shown for sulpharsphenamin in treatment of cases of **neurosyphilis**. Evidence was not obtained that the drug influenced favorably the clinical course of patients with syphilis of the **cardiovascular system**. The drug was found useful in treating 3 patients who had previously developed "shock" or "nitritoid" reactions after intravenous injections of the other arsphenamins. Intramuscular injection seemed to be of considerable importance as far as systemic toxic reactions were concerned, being the method of choice. Dermatitis was found to have a relatively high incidence, showing a total of six cases in 678 injections. It is important that three of these occurred among the 110 injections administered intravenously as compared with only one among 302 given intramuscularly. J. C. Fox (Am. Jour. of Syphilis, July, 1925).

Very good results were obtained by the writer from the intravenous use of sulpharsphenamin. In cases of syph-

ilis which are Wassermann-negative and free from clinical symptoms, sulpharsphenamin seems quite as capable of controlling the disease as the older arsenicals. In **neural syphilis** sulpharsphenamin is even more effective than arsphenamin or neoarsphenamin. Given intravenously, sulpharsphenamin did not produce dermatitis and caused practically no constitutional reactions. On account of the absence of disagreeable reactions patients submit more willingly to treatment with sulpharsphenamin, and, consequently, it is indicated in cases in which the maximum spirocheticidal effect of arsphenamin and neoarsphenamin is not essential. Lautman (Arch. Derm. and Syph., Feb., 1926).

*Primary Stage.*—As there is a distinct possibility that, if arsphenamin is injected in the primary stage of the disease, the infection will be entirely overcome, and since conclusive laboratory methods of confirming a diagnosis of syphilitic chancre are now available, the course formerly recommended, *viz.*, waiting for secondaries to appear before beginning treatment, is no longer justified. In cases where the surgeon is not convinced from the appearance of the lesion that it is syphilitic, little or no difficulty will be experienced in examining scrapings from the sore by the dark ground, India ink, or other methods for the detection of the organism—*Spirochata pallida*. Where doubt is occasioned owing to the presence of a double chancroidal and syphilitic infection, it will soon be dispelled through the fact that the lesion will not heal, or will improve only temporarily, under the usual treatment for chancroid. Upon continued observation—until the incubation period of the chancre has expired—further local disturbance will be observed.

For the reasons above mentioned, an injection of arsphenamin (or neoarsphenamin) should be given at the earliest opportunity in primary syphilis. In a few days the sore will have healed. The Wassermann test should be tried two days after the injection and, if the test is positive at that time, further treatment should be given, *viz.*, another injection of the drug after a suitable interval, followed by mercurial treatment—preferably by inunction. Intravenous injections are much more rapid in their action on the chancre and in causing the spirochetes to disappear than intramuscular injections; hence they should be given the preference. Excision, cauterization or mercurial inunctions of the chancre are no longer deemed advantageous measures in incipient syphilis.

Of the primary and secondary cases among 350 **syphilitics**, not one failed to clear within a month after salvarsan; nearly all in a week to ten days. A little pigmentation was not infrequently left, but this cleared gradually without further treatment. In no primary case did a secondary rash develop. Tertiary cases, including huge ulcerations with splinters of dead bone at the base, and measuring in one case over two inches across, cleared, granulated, and healed as fast as epithelium could grow over. Congenital cases are more obstinate, especially **interstitial keratitis**, but even this certainly improves. **Tabes**, except in the late stage, seems greatly to benefit. Not one lesion in the 350 cases resisted more than three injections, though among them were numerous patients treated for a long time, thoroughly but unsuccessfully, with mercury. There were about 20 recurrences, all treated early with small doses, intravenous or intramuscular, and 2 only with three injections given intravenously; in each of these latter cases the dose given was

0.4 Gm. or under. Molesworth (*Austral. Med. Gaz.*, Aug. 3, 1912).

In the early period it may be possible with one, two, or three doses to eradicate the infection. During the secondary stage it is more difficult, and in the still older ones still more of the drug must be used. The initial dose for men should not exceed 0.4 Gm. and 0.3 Gm. for women, until the susceptibility has been tested. In the early stage three or four doses, supplemented by mercury, will in many cases cure the disease in from six months to a year. The florid stage requires more intensive treatment—five or six doses followed by several mercurial courses are necessary. J. A. Fordyce (*Jour. Amer. Med. Assoc.*, Oct. 5, 1912).

The author recommends 3 full doses of salvarsan in the primary stage, the first 2 one week apart and the third 2 weeks from the second. Mercury is begun immediately or preceding the first salvarsan. From 1 to 2 grains (0.065 to 0.13 Gm.) of one of the insoluble salts is given twice weekly for four doses; then at weekly intervals for 6 weeks, making 10 doses in all. No further treatment is given for 2 months. The Wassermann is then taken. If negative, another full dose of salvarsan is given and blood taken 24 hours later for a second Wassermann. Even though the Wassermann is negative after the provocative salvarsan injection the second course of treatment is given. It consists of another dose of salvarsan in 3 weeks and, subsequently, 6 mercury injections. No further treatment is given, but the patient is watched for a year. If positive, the courses are continued as at first, but salvarsan is given at 2-week intervals. After repeated courses of mercury injections, a short course of potassium iodide is indicated. J. L. Murray (*Ohio State Med. Jour.*, Sept., 1917).

In the primary stage, the writer counsels the following: **Neoarsphenamin**, 0.9 Gm., or **arsphenamin**, 0.3 Gm., intravenously twice a week for 2 weeks, then once a week for 6 weeks;

at the same time, inunctions of 50 per cent. **mercurial ointment** on alternative days, continued up to 30 inunctions; repeat entire course after a rest of 3 weeks; another 3 weeks' rest; if Wassermann is then negative and no evidence of syphilis exists, **mercury** by mouth (or injections or inunctions) to be taken 3 weeks out of 4. It is suspected that generalization of infection may take place even though the Wassermann does not become positive for a year. Schamberg (Penna. Med. Jour., Jan., 1922).

The abortive treatment should consist of about 10 intravenous **arsphenamin** injections of 0.2 to 0.4 Gm. each, with a suitable **mercury** preparation given simultaneously in the same syringe. A positive Wassermann does not necessarily preclude successful abortive treatment. When the arsenical is begun within 3 weeks after infection, 90 per cent. of cures can be expected; if in 4 weeks, 75 or 80 per cent.; if in 5 weeks, 50 or 60 per cent., and if in 6 weeks, 40 per cent. Several after-treatments should be given even after apparently successful abortive treatment. R. Polland (Wien. klin. Woch., Feb. 14, 1924).

**Secondary Stage.**—In secondary cases Schamberg advocates 3 courses of the **arsenical** and **mercurial** treatment above referred to during the first year and 2 during the second. In the intervals **mercury** may be taken by mouth. There has been too much tendency to regard a negative Wassermann as evidence of extinction of the infection. Not infrequently it is negative in the presence of a circumscribed tertiary skin lesion or in certain cases of visceral syphilis. Early negative Wassermanns after brief treatment should be disregarded. Every patient must receive an irreducible minimum of treatment, otherwise his future is uncertain. Wassermanns should be taken from time to time for 2 years, and **mercury**

continued even in the face of a negative outcome.

There is no uniformity of opinion as to a standard treatment of syphilis. Many give 0.4 to 0.6 Gm. of **arsphenamin** or 0.75 to 0.9 Gm. of **neoarsphenamin** weekly, in conjunction with **mercury** injections or inunctions, continued for 6 weeks, followed by a month's rest, then other courses. Pollitzer has advocated 3 successive daily doses of **arsphenamin**, 0.4 to 0.6 Gm., or **neoarsphenamin**, 0.9 Gm., followed by weekly intramuscular injections of **mercury salicylate** for 8 weeks; a month's rest; repetition of treatment; 2 months' rest, and a third course. The French often give ascending weekly doses of the **arsenicals**, 0.1, 0.2, 0.3, up to 0.6 Gm., to avoid complications from hypersusceptibility. Vigorous associated use of **mercury** may readily irritate the kidneys, reduce arsenic elimination, and thus react on the liver. Combined **arsenical** and **mercurial** treatment is no doubt more active and rapidly curative than either drug alone, but intramuscular injections of insoluble **mercury** should not be given during the regular **arsenical** treatment. (Schamberg.)

Conservative method of **arsphenamin** therapy in **syphilis** strongly advocated, on the basis of 1133 cases of syphilis, involving 10,589 serological examinations. Of the 456 cases under observation sufficiently long to permit of deductions, 367, or 80 per cent., were clinically and serologically negative for 2 or more years, this negative phase being reached by 154 cases with only 1 administration of **arsphenamin** or **neoarsphenamin**, and in 107 cases with only 2 administrations. Every case received a full commensurate dose of **arsphenamin** (0.6 Gm.—10 grains) which was not repeated for 4 to 6

months, except in the face of a threatening and serious clinical manifestation. A serological examination was made every 30 days for the first 6 months. If there was no material change for the better, or the serological examination showed a relapsing character, treatment was repeated at the end of the first 4 months. If the serological examination showed improvement but was not negative, or if there were fairly well defined clinical manifestations, treatment was invariably repeated in 6 months. This plan was continued until the patient became persistently serologically negative and devoid of all clinical manifestations. Good results are obtained if antispecific remedies are entirely removed for a period of several months and temporarily replaced by general tonic treatment. The author decries particularly the long-continued administration of small fractional doses, a form of treatment especially prone to establish arsphenamin tolerance. M. L. Heidingsfeld (*Jour. Amer. Med. Assoc.*, Aug. 10, 1918).

Injections of arsphenamin given at 72-hour intervals in selected cases. Ninety-eight injections were given to 22 patients. There was no untoward result, though a number gave the usual reactions of nausea, vomiting, diarrhea, and headache. The dose of the drug employed was 0.4 Gm. per 150 pounds of body weight, given in 70 c.c. (2½ ounces) of distilled and double boiled water. All injections were given in the office and the patient allowed to go home immediately. In 18 of the 19 patients with positive Wassermanns, the reaction promptly became negative. Hazen (*Amer. Jour. of Syphilis*, Oct., 1918).

The skin and mucous membrane lesions of the secondary type rapidly disappear under arsphenamin. Macular eruptions begin to fade within twelve hours after an intravenous injection and a few days later are entirely gone. Mucous patches, condylomata, and secondary periostitis likewise

often disappear in two or three days, —a much shorter period than is the case with mercurial treatment. Papular eruptions are not so promptly removed, especially when the individual lesions are of large size, and after they have been overcome pigmented spots may persist for some time at their sites. Pustular lesions show prompt improvement, however, especially if suitable local detergent and antiseptic treatment is simultaneously applied. Recurrent syphilides, including lichen syphiliticus, generally disappear more rapidly than the first, though the papular and squamous forms may still prove obstinate. Other manifestations of secondary syphilis, such as joint and bone pains, nocturnal headache, and alopecia come to an abrupt standstill when arsphenamin is given.

The author made 516 injections of salvarsan in 395 patients, of whom 382 were syphilitic. The majority of the injections (396) were made intravenously. With the exception of 37 recurrences, the results were very satisfactory. In 2 cases of syphilis complicated, 1 by a grave nephritis and the other by diabetes, repeated injections of fractional doses of salvarsan were not followed by any reaction. Neither the nephritis nor the diabetes was benefited. Two patients with **relapsing fever** recovered, the spirochetes disappearing eight hours after the injection. In 1 case of tuberculosis of the throat and in 2 cases of cerebral tumors the results from treatment with salvarsan were negative. Galpern (*Roussky Vrtch*, June 16, 1912).

Intense **headaches**, often so persistent during the secondary and tertiary stage, of the disease and due to a low-grade meningitis, usually remit with remarkable rapidity under salvarsan. J. A. Fordyce (*Jour. Amer. Med. Assoc.*, Oct. 5, 1912).

Especially remarkable are the results obtained in the "malignant" forms of syphilis in which mercury has failed and the patient is suffering from anemia, severe ulcerations of the mucous membranes, and gummata of the skin. Cases of syphilis complicated with tuberculosis of the lungs have been reported in which arsphenamin produced an excellent effect on both diseases.

Cases of **syphilis** complicated by **pulmonary tuberculosis** should receive salvarsan, which is not only of value in improving the syphilis, but actually by its good effect on metabolism benefits the tuberculosis. Where cavities are present in the lungs intramuscular rather than intravenous injections should be employed. S. Pollitzer (N. Y. State Jour. of Med., June, 1911).

**Tertiary Stage.**—In this stage intensive treatment is ordinarily to be avoided, for rapid cure is unlikely and powerful remedies may do actual harm. Moderate doses of **arsphenamin** may be given and followed by small doses of **mercury**. The **iodides**, while not directly spirocheticidal, have an admirable influence. Sometimes suspension of specific medication and correction of digestive, nervous or other disturbances is of great advantage. Patients over 50 years of age without evidence of active visceral or neurosyphilis should not be vigorously treated even though they have a strongly positive Wassermann. At all times, careful attention should be paid to danger signals such as renal irritation, jaundice, and itching or cutaneous eruption.

Under the influence of treatment, particularly with salvarsan, the specific infiltrations persist for some time, though the diffuse leucocytic infiltrations disappear more rapidly. The

early institution of treatment and the administration of salvarsan at frequent intervals markedly influence the quality and rapidity of disappearance of the infiltrations. Endarteritic changes are strikingly affected by treatment. Following salvarsan, the elastic fibers undergo further injury, and may disappear entirely; in other words, elastic tissue is less affected by the living spirochetes than by their endotoxins. Rohrbach (Munch. med. Woch., Bd. lix, S. 967, 1912).

Arsphenamin also causes a great improvement in the patient's general state, bringing about an increase in the body weight, a subjective feeling of marked physical and mental betterment, increased appetite, and relief from such complaints as headache, giddiness, precordial pain or oppression and palpitations (McDonagh). As in the secondary stage, obstinate ulcerations of the pharynx and larynx, causing dysphagia and sometimes pronounced stenosis of the respiratory passages, can be promptly relieved with the remedy. Such uncommon but troublesome manifestations as serpiginous syphilides, chronic glossitis, Ménière's syndrome, pulmonary syphilis, and syphilitic arthritis can be more or less rapidly overcome by intravenous injections of the drug.

In the tertiary stage the infecting cause is not readily attacked, as the lesions are in the deeper, firmer structures. Large doses of salvarsan are not indicated, except in very rapidly progressive and destructive lesions. It should rather be given so as to be effective constantly, i.e., the dosage should be small, 0.3 Gm. given once a week, or once in two weeks. As salvarsan has no action in breaking down pathological tissue, it is necessary to give the iodides, which should be administered in increasing dosage except in laryngeal conditions in which much narrowing of the lumen is present.

When the patient appears cured, the iodides should not be discontinued, but given regularly, whereas salvarsan should now be given every six or eight weeks in the dose of 0.3 Gm. for several doses. Then all medication should cease and blood examinations be carried out every five or six weeks for several months. F. W. White (Laryngoscope, Sept., 1912).

According to McDonagh, any case of tertiary syphilis can be cured if the treatment is carried out with sufficient energy and persistence,—at least a permanently negative Wassermann reaction can be secured. In tertiary cases where there are no symptoms but the Wassermann is positive, salvarsan is hardly necessary; for if symptoms appear at any time, they can be quickly eradicated with the drug. In patients coming under observation with definite tertiary symptoms, however, salvarsan, mercury, and potassium iodide may be used simultaneously.

To render the Wassermann constantly negative in these cases, about 3 Gm. of salvarsan will, in general, be required.

In a comparative study, salvarsan was given intravenously in an initial dose of 0.3 Gm. (5 grains) and in subsequent doses of 0.6 Gm. (10 grains); neosalvarsan, in 0.45- and 0.9- Gm. (7 and 14 grains) doses. The disappearance of the lesions was equally rapid and complete. Reactions were much more frequent after salvarsan than neosalvarsan. Serologically, neosalvarsan seemed decidedly the better drug, there being 40 per cent. of negative reactions as against about 7 per cent. A course of 4 injections of either drug alone is insufficient treatment, and should always be followed by mercurial treatment. More than 4 doses of the arsenical should also usually be given.

Trimble and Rothwell (Jour. Amer. Med. Assoc., Dec. 30, 1916).

Favorable report on silver-sodium salvarsan, placed on the market by the bacteriologist Kolle. The product possesses an energetic action in much smaller doses than neosalvarsan. This higher efficiency is due to the combination of metallic silver with the salvarsan. Galewski (Deut. med. Woch., Nov. 28, 1918).

*Lesions of the Organs of Special Sense.*—Although the occasional apparent untoward effects of salvarsan on certain of the cranial nerves at first tended to discount its value in syphilis of the special sense organs, subsequent experience fairly definitely showed the drug to be equally as useful in involvements of this nature as in overcoming the superficial—skin and mucous membrane—manifestations of the disease. Such serious phenomena as **iritis, iridocyclitis, interstitial keratitis, optic neuritis, neuroretinitis, chronic otitis media and deafness, aphonia, syphilitic nasal catarrh, and progressive deformities of the nose and palate**, alike yield more or less rapidly to arsphenamin.

Many of the so-called bad results of injections of "606" are similar to the lesions which one might quite easily find in the ordinary course of syphilitic infections. The best results from its use were obtained in cases of iritis, but lasting good resulted in 1 case of typical **heredo-syphilitic keratitis**. F. de Lapersonne and André Léri (Arch. d'ophtal., Jan., 1911).

Salvarsan is very effective in secondary and tertiary manifestations of the uveal tract. It causes no appreciable subjective or objective symptoms on the healthy eyes of syphilitics. Rosenbaum (Med. Rec., July 22, 1911).

Eye cases classified into three groups: those in which good results are produced, those in which the re-

sult is doubtful, and those in which the effect of salvarsan is neutral. To the first group belong **iritis** and **iridocyclitis**, as well as probably descending **optic neuritis** and **atrophy**. Doubtful cases are those of choked disk and certain cases of ascending neuritis. No benefit can be expected in vitreous opacities, nor in old myosis or mydriasis. Dolganoff (Berl. klin. Woch., Nov. 6, 1911).

The author has given salvarsan, with rapid and marked benefit, in several cases of **retinochorioiditis** with sudden blindness. When the optic nerves are diseased, even in an advanced stage, and in emergency conditions, he does not fear to administer salvarsan; but he gives it only intravenously, as all the cases of involvement of the cranial nerves following the use of salvarsan have occurred where the drug had been used intramuscularly. Neuritis of cranial nerves after salvarsan is merely coincidental and only a syphilitic inflammation of the nerve proper without connection with the arsenic. Yet it is a wise precautionary measure to have an ophthalmoscopic examination made preceding the intravenous use of salvarsan. J. L. Boehm (N. Y. Med. Jour., Dec. 2, 1911).

Report of 2 cases of **acute iritis** with condyloma, in which there were rapid subsidence of the inflammatory symptoms and disappearance of the condyloma following injection of salvarsan. The treatment caused entire disappearance of the inflammatory symptoms in eleven days in a case of chronic general **uveitis**. In a case of a low form of long-continued general **uveitis**, there was no immediate result. In 4 out of 5 cases of **interstitial keratitis** treated, there was a rapid disappearance of circumcorneal injection, photophobia, and lachrymation. In 3 cases there was no exceptional rapidity in the clearing of the corneal infiltration. F. E. Cheney (Boston Med. and Surg. Jour., Dec. 21, 1911).

Salvarsan is of value in **syphilis** of the **ear**, especially in recent aural

lues. In old aural lues its use should be guarded, especially if there is degeneration of the cochlear or vestibular nerves. If it is injected while the child is young, it may be useful in congenital deaf-dumbness. Voorhees (Amer. Med., July, 1912).

**Syphilitic lesions in the throat** healed with remarkable rapidity under salvarsan, although most of them had resisted treatment by the older methods. Laryngeal syphilis has shown less marked improvement, owing perhaps to ulceration, scar tissue, ankylosis of the arytenoids, etc. F. C. Cobb (Laryngoscope, Sept., 1912).

Neosalvarsan preferred for affections of the anterior parts of the eye, and salvarsan for affections of the retina and optic nerve, especially when the nervous system is attacked in any way. J. Igersheimer (Ophthalmoscope, Nov., 1912).

Occasionally, resistant ulcerations (particularly those of the pharynx) are met which improve up to a certain point, and then cease to improve under salvarsan only to yield to vaccine treatment. Sometimes a case with well-marked polymorphic rash is seen, and the entire eruption is looked on as syphilitic. Salvarsan is given, and after one or two injections almost the whole rash is gone, but patches of eczema or some other type of rash are left. L. Kilroy (Lancet, Feb. 1, 1913).

In ocular syphilitic lesions the writer's procedure in treatment, from the time the disease has become generalized, *i.e.*, after 40 days have elapsed, consists in first giving a daily intravenous injection of mercury cyanide, 0.01 Gm. ( $\frac{1}{10}$  grain), for 4 days; then, 10 injections of neoarsphenamin, in weekly injections increasing from 0.15 to 0.9 Gm.; between these, mercury cyanide, 0.01 Gm., every other day, and once weekly, 6 drops of arquéritol (a gray oil and silver preparation) intramuscularly. Three such courses are given in the first year, with rest intervals of 1 month and 2 months. The second year 3 series of 8 injections of neoarsphen-

amin are given, and the third year, 3 series of 6 injections, with mercury cyanide between as before. Blanchard (Ann. d'ocul., Sept., 1924).

The so-called "*neurorecurrences*," consisting usually of lesions of the auditory and optic nerves appearing after a single injection of salvarsan, and which have been the subject of much discussion, are no longer considered due directly to the action of the drug—as was the case with atoxyl and arsacetyl—but to a temporary accentuation by the drug of syphilitic nerve-lesions previously present. Only in 1 case—that of Finger—in a series of 30,000 patients with previously healthy eyes, treated with salvarsan, did Ehrlich find optic atrophy. In this instance the patient had received previous treatment with the other arsenicals; hence it is recommended not to use salvarsan where atoxyl or related compounds have already been administered.

The "*neurorecurrences*" appear especially in early syphilis, and rather constantly within a period of several weeks after the injection. It is generally recognized—withstanding the fact that greater care in the observation of the cases is now customary than formerly, and some cases are now recorded which would most likely have been missed in earlier years—that these "*relapses*" do occur after salvarsan oftener than otherwise, and must in some way, at least in a certain proportion of cases, be referable to the drug. Where the cochlear nerve alone is involved, deafness, either rapid or gradual, is complained of, while if the vestibular nerve is at fault there occur dizziness, tinnitus aurium, nystagmus, and vomiting. The ocular complications

lead to headache, photophobia, conjunctivitis, and dimness of vision. Other cranial nerves sometimes involved are the facial, oculomotor, trochlear, abducens, and trigeminal.

Inflammation of the optic, auditory, facial, and other cranial nerves has developed in a minute percentage of cases after the use of salvarsan in syphilis. The same complications may occur spontaneously or after the use of mercury. A risk is incurred in discontinuing antisyphilitic treatment for a long period in early syphilis, after a single injection of salvarsan, particularly when given subcutaneously or intramuscularly. Schamberg (Jour. Amer. Med. Assoc., May 20, 1911).

Salvarsan has a favorable effect on the secondary aural affection in that it eliminates the primary focus of the disease, *e.g.*, the plaques in the throat, and is therefore preferable to mercury in certain cases. Wherever the internal ear is normal, there are no otic contraindications to salvarsan.

It is almost pathognomonic that ear affections appearing independently of cutaneous symptoms occur four to eight weeks after the injection of the salvarsan. A second dose of salvarsan is contraindicated in such cases of nerve affection. The safest therapy is a strong mercurial treatment.

In otosclerosis the nerve-elements of the ear are involved in the pathological processes and salvarsan is contraindicated. In 2 cases the hearing, according to the patients, grew rapidly worse after salvarsan.

Whether salvarsan is indicated in hereditary luetic deafness is still an open question, for, on the one hand, considerable improvement in the functional activity of the ear has been noted, and, on the other, an equally marked deterioration. Oscar Beck (Laryngoscope, Sept., 1912).

That these disturbances are not due directly to the drug is indicated by the fact that they are usually im-



proved or entirely overcome by further injections of salvarsan or by mercurial treatment. Roscher advises the routine administration of mercury before the former drug is given at all, in secondary stage cases with well-developed lesions, while McDonagh states that since making it a rule to repeat salvarsan within an interval of a few days, and to combine it with mercury, he has had no more cases of cranial neuritis.

Cases of permanent involvement of the auditory, ocular, and other cranial nerves, even where salvarsan had been repeated, have been met with, but their number is small in comparison with that of cases similarly afflicted which have not been treated with salvarsan (Carpenter).

The partial non-success of salvarsan in lues is due not to the drug, but to the disease—foci hard to penetrate or reach, local reactions due to setting free of the endotoxins. Improvements are not to be sought in a new drug, but in improved modes of application of the present one. P. Ehrlich (*Münch. med. Woch.*, Nov. 21, 1911).

Aural symptoms non-specific in origin do not contraindicate the administration of salvarsan, and if they are caused by some process specific in nature they furnish a positive indication for it. The contention of some that the remedy is not to be given in mild degrees of impairment of hearing or in unilateral deafness on the ground that it is liable to destroy the remaining hearing power is not supported by the facts. C. E. Perkins (*Laryngoscope*, Sept., 1912).

Report of 5 cases, 3 of which strengthen the view that salvarsan may be specially harmful to nerve tissue. The fourth patient returned with acute iritis within 6 months after a negative Wassermann had been produced by salvarsan, and this iritis yielded at once to mercury.

There had been no chance of reinfection. The fifth case likewise was pronounced cured, with a negative Wassermann, but within 18 months he was suffering from acute choroidoiritis. In interstitial keratitis mercury has given the writer much better results. Treatment with salvarsan is not devoid of danger, and has not been proved superior to mercury. Fergus (*Arch. of Ophthalm.*, Jan., 1918).

The immediate cause of the neurorecurrences, which are generally unilateral, appears to be usually an inflammation of the trunks of the cranial nerves concerned. The consequent enlargement is believed to bring about pressure upon the nerves at points where the surrounding tissues—as in bony canals—are unyielding, functional paresis or paralysis being the result. The inflammation itself, in turn, is probably due to the activity of spirochetes locked up in the nerves and not killed—but perhaps, on the contrary, stimulated—by the first injection of salvarsan. That the Wassermann reaction in these cases is negative seems due to the fact that the organisms locally present are not numerous enough to bring about antibody formation and itself also tends to substantiate the assumption that these organisms are in a sequestered and sheltered situation where it is difficult for the salvarsan to reach them in sufficient amount.

Early neurorecurrences are due to acute edema resulting from rapid death of spirochetal foci (particularly in nerves running through a rigid canal, like the auditory nerve), and can be compared to the erythematous skin eruptions noted where drugs are given. In a large series of cases observed, 194 early neurorecidives occurred after salvarsan injection, and 123 after mercury injections,—no very great disproportion. Late recurrences in the nervous system are due

to the fact that all but a few spirochetes, at some site not readily reached by the arsenic, have been killed, and that these organisms then have the opportunity to grow unhindered with greatly increased rapidity. Such nervous recurrences take place almost exclusively in the early secondary period, when there are most spirochetes in the body. That the arsenic is not at fault is shown in that they do not take place in the early stages of syphilis; that the nervous symptoms are cured by salvarsan; that in other spirilloses (frambesia, recurrent fever, etc.) no toxic symptoms ever arise. P. Ehrlich (Munch. med. Woch., Nov. 21, 1911).

Neurorecidives after salvarsan treatment vary markedly in the different clinics and seem to be particularly conspicuous in certain quarters. This gives rise to the suspicion that Ehrlich's injection rules are not followed scrupulously. When the solution is not injected immediately after its preparation, or when the solution during its preparation is stirred too vigorously, oxidation products are formed, much more poisonous than salvarsan, which probably have an affinity for the central nervous system. Cronquist (Munch. med. Woch., Nov. 12, 1912).

#### *Syphilis of the Nervous System.*—

In nervous conditions dependent on syphilis the efficacy of salvarsan depends upon whether the condition present is merely one of inflammation with a possibility of complete resolution or has already led to destruction of nerve-cells. Among the first category are cases of **cerebral or cerebrospinal syphilis**, associated with a **cortical or basal syphilitic meningitis**, and manifested by headache, insomnia, irritability, psychic disturbances, dizziness, epileptic seizures, signs of involvement of cranial or spinal nerves, such as **ophthalmo-**

**plegia**, etc. These are the disturbances which generally occur within a few years after the infection and develop with considerable rapidity. In these the administration of salvarsan in doses not exceeding 0.3 Gm. will generally produce a notable and sometimes a most striking improvement. This drug should not be given, however, until after the stage of acute inflammation has passed, for a fatal ending, owing to primary aggravation of the process and pressure on intracranial centers, has been known to occur where this rule has been disregarded. Even at best, convulsive phenomena and temporary local paralyses may follow the administration of the drug. In recent cases of hemiplegia due to thrombosis, salvarsan should not be given, as there is danger of an excessive inflammatory reaction and of hemorrhage due to softening of the thrombus. Mercury unctions should be used instead, and salvarsan not resorted to unless mercury loses its effect (McDonagh).

Case of severe **trigeminal neuralgia** in a woman who had never had any symptoms of syphilis, but whose serum gave a positive reaction, which was cured after an intramuscular injection of 0.5 Gm. in clear alkaline solution. Severe neuralgic pains in the legs in 2 syphilitics, twenty years after infection, disappeared after one intravenous injection of 0.4 Gm. in each case. Browning and McKenzie (Brit. Med. Jour., Sept. 23, 1911).

Seventy-five patients suffering from **syphilitic nervous disease** treated with salvarsan. The treatment is effective, but in order to get its best results large doses must be given and frequently repeated. Of 36 cases of **tabes** in various stages 22 showed striking and some remarkable improvement, both subjective and objective. In 2 cases the pupils re-

gained their capacity to react to light. The results were incomparably better than those obtained by mercury. Salvarsan was given in 9 cases diagnosed as **general paresis**. In 2 doubtful cases and 1 undoubted case of **paresis** great improvement took place. Gratifying response was observed in cases diagnosed **meningitis** and **meningomyelitis**. In only 2 out of 6 cases of **cerebral endarteritis** of luetic origin was any perceptible improvement observed.

The average dose of salvarsan for an individual suffering from diseases of the central nervous system whose vitality is not conspicuously impaired is 0.6 Gm. In patients whose blood-pressure is high (above 165 mm. by the Stanton apparatus) and in whom there is very distinct evidence of cardiovascular degeneration, not more than one-half a dose should be given the first time. If the first administration is not followed within a fortnight by a chemical and microscopic evidence of cessation of activity of the syphilitic poison and the pathological process conditioned by it (negative Wassermann reaction, diminution of globulin, profound numerical reduction of lymphocytes in the cerebrospinal fluid), the dose should be repeated. The second dose should be the same as the first, unless some special reason exists for increasing or diminishing it. On the other hand, if the first dose is followed by indications of cessation of activity of the pathological process, the second dose should be delayed for from six weeks to three months.

One feature of salvarsan therapy of organic nervous diseases is the enormous physical uplift which many patients get, shown not only by a feeling of well-being and improvement, but by an increase of weight. Collins and Armour (*Jour. Amer. Med. Assoc.*, June 22, 1912).

Excellent results obtained with salvarsan in 48 cases of various syphilitic affections of the central nervous system. In **lues cerebri** there was improvement or disappearance of

facial paralysis and hemiplegia in 66 per cent. of the cases. Contractures disappear and convulsions are soon checked. Writing and general muscular power will approach the normal and pain and the paresthesia are alleviated. In 10 cases the psychic condition became normal and in 2 there was considerable improvement. In cerebrospinal lues, the gait was restored in 25 per cent. and there was decided improvement in the bladder and sexual functions. The general condition was usually influenced to a marked degree. In the initial stages of **tabes** the patellar reflexes may return and the ataxia, Romberg's symptom, gastric crises, lancinating pains and other pains may disappear entirely. In **dementia paralytica**, in the beginning stages, the pupillary reaction returned in 3 out of 28 cases and the tendon reflexes in 1 case. In 4 cases the gait was improved and in 11 cases the speech became more distinct. In a fair percentage, memory and the general intelligence returned, while in 3 cases the patients could again return to their vocation. Mercury and potassium iodide should be used in combination with the salvarsan, and in parietic dementia it is of advantage also to employ injections of sodium nucleinate. J. Donath (*Münch. med. Woch.*, Oct. 22, 1912).

Lumbar puncture in 115 syphilitic patients showed that the pressure of the fluid and lymphocyte count present changes, sometimes very marked, in the preroseolic period and, especially, in the early secondary period. These correspond to a meningoen- cephalitis, and are sometimes accompanied by symptoms such as headache, vertigo, hyperacusia or hypacusia, and evidences of paresis or paralysis of the oculomotor or facial nerves. From 7 cases, in each of which two or more lumbar punctures were practised, before and after repeated salvarsan injections, the author concludes that the nervous condition is probably favorably influenced by this remedy. The neurorecurrences are looked upon by the author as

evidences of diffuse or localized syphilitic meningitis, rather than of the action of salvarsan. They can be cured or improved provided they are detected early, through close observation of the patient, including the cerebrospinal fluid, and combated promptly and persistently. Dind (*Revue méd. de la Suisse Romande*, March, 1913).

Case of **brain syphilis** in a state so desperate that in spite of the contraindication, salvarsan was used. Rapid and complete recovery took place. Eddy (*Jour. Amer. Med. Assoc.*, Apr. 26, 1913).

In **syphilis of the nervous system** the writers report good results from intravenous injections of arsphenamin in increasing doses, each followed in 5 minutes by lumbar puncture, evacuating at least 10 c.c. (2½ drams) of cerebrospinal fluid. This method ranks next to intraspinal injection of arsphenaminized spinal fluid, and is safer than the latter when there is doubt as to the soundness of the neuraxis. Tzanck and Bernard (*Paris méd.*, May 11, 1918).

Arsphenamin may act very satisfactorily in almost any form of neurosyphilis. For best results, it is often necessary to use it twice or three times a week over a good many months. Until this has been done it has not been demonstrated that the drug will not give a satisfactory result. Many times, however, it is ineffectual. In a fair number of such cases, intraspinal, intracisternal, or intraventricular injections may do better. Except in very mild meningeal neurosyphilis, it is not to be expected that spinal fluid changes will begin to occur for at least 3 months, and often it takes 6 months to 1 year for them to be considered definite. In parietic neurosyphilis, a combination of routes should be used. Solomon (*Boston Med. and Surg. Jour.*, Aug. 27, 1925).

In **tabes dorsalis** salvarsan is somewhat more than a palliative, though naturally incapable of causing regeneration of destroyed nerve-cells. It tends to relieve certain of the symp-

toms, but in many instances only temporarily. With repeated small doses of salvarsan more can be accomplished in this disease than with mercury and iodides. In cases with negative Wassermann reaction, however, its use is not advised. More marked results than in tabes are obtained in cases of cerebrospinal syphilis simulating the latter in their symptomatology.

The author has several cases of **tabes** and of **syphilis of the central nervous system** on record where a combination of salvarsan with mercury did more good than either drug alone. He has, therefore, made it a rule to use both drugs in these cases. O. L. Klieneberger (*Berl. klin. Woch.*, March 4, 1912).

Salvarsan brings the **tabetic process** to a standstill. Furthermore, it can cause retrogression of certain lesions in the spinal roots or in the cord itself. The improvement is noticeable in the disappearance of the later symptoms and also, in some cases, of the older symptoms. The author observed a series of patients for two and a half years, and in a few cases the patients were completely cured. Leredde (*Münch. med. Woch.*, Sept. 24, 1912).

Salvarsan is indicated in **tabes** with a very positive serum reaction and a lymphocytosis of the cerebrospinal fluid; it should be given in repeated small doses at proper intervals. J. A. Fordyce (*Jour. Amer. Med. Assoc.*, Oct. 5, 1912).

Where a **syphilitic meningitis** exists in **tabes** one can expect brilliant results from salvarsan as far as the symptoms due to the meningitis are concerned, and in early cases of tabes one can hope for a remission in the progressive course of the disease. A man, 45 years of age, with a history of syphilis seventeen years previously, had complained of pains in the arms and limbs for some three months, more pronounced in the

upper extremities. Reflex immobility of the pupils, vesical atony and girdle sensation were present, together with paresthesias and moderate analgesia and loss of deep-pressure pain sense in the lower extremities. Ataxia was absent, and the tendon reflexes were exaggerated. He had been impotent for some years. In this case the salvarsan cleared up the pains entirely, the exaggerated reflexes subsided, and the patient gained some twenty-five pounds in weight in the course of six months. The pupillary findings, analgesias, loss of deep pain sense, loss of the left Achilles reflex, and slowing of urination remain. The patient feels well and is engaged in business life. G. A. Young (*Western Med. Rev.*, Feb., 1913).

While some slight improvement has followed the use of salvarsan in a few cases of *tabes*, the drug when pushed has intensified the destructive action of the disease and hastened the death of the patient. E. H. Trowbridge (*Jour. Amer. Med. Assoc.*, Feb. 8, 1913).

Report of a case without syphilitic history, but giving a positive Wassermann reaction, that showed the characteristic symptoms of *tabes*. It was first treated with mercurial inunctions and iodine; the patient was then given 0.6 Gm. of salvarsan, which was repeated some two and a half months later.

A month afterward, examination showed absence of the Argyll-Robertson pupil, improvement in the coordination, and less marked Romberg sign, together with gain in weight and a general feeling of well-being. J. J. Zaun (*Jour. Amer. Med. Assoc.*, March 1, 1913).

Many patients with **syphilitic conditions of the cerebrospinal system** are aggravated by one or two doses of salvarsan, while, on the other hand, many of their symptoms are relieved by the persistent use of the drug. The pains, crises, bladder symptoms, and general nutrition are often

greatly benefited. The author's plan of treatment in these cases is to give injections of salvarsan at weekly intervals, combining them with mercury at intervals of three or four days. In 1 case of paresis he gave twenty-one injections of salvarsan, about 10 Gm. in all, with marked alleviation of the symptoms. The Wassermann reaction in this case had not been influenced by the treatment. He is becoming more and more convinced that salvarsan has no deleterious effect on the optic nerve, having, on the contrary, 2 cases under observation where it proved distinctly beneficial. In 1 of these cases the visual fields have enlarged. J. A. Fordyce (*Jour. Amer. Med. Assoc.*, May 17, 1913).

The writer advocates intramuscular use in *tabes dorsalis* when but 1 symptom of the disease is in evidence, as intravenous administration may provoke appearance of its other manifestations. J. Bejarano (*Rev. esp. de urol. y derm.*, Apr., 1924).

**General paralysis** is less amenable to salvarsan than *tabes*, though occasionally some symptomatic improvement is brought about. It is the consensus of opinion that the drug is of value only in the earliest stages of this disorder, and that its use in more advanced cases is attended with danger. In any event, only half a dose of salvarsan should be given, as in *tabes* and brain syphilis.

Case of a man, 40 years old, who began to suffer from dementia parietica; 0.5 Gm. of "606" was injected into the muscles beside the left scapula. For forty-eight hours he seemed to do well, then his temperature rose, his pupils became moderately contracted; then his feet and hands began to tremble, he could not stand, and he began to perspire freely. He lost his strength completely, though there was no paresis or edema and the tendon reflexes were lively. The heart and lungs showed no organic

trouble, but he sank until death occurred. Autopsy revealed only a slight acute parenchymatous degeneration of some organs, particularly the kidney, and fatty degeneration of some fibers of the vagus and of the nerves in the right brachial plexus that could be ascribed to the poisoning with arsenic. The changes typical of dementia paretica were present in the brain. Jørgensen (Med. Klinik, March 5, 1911).

Fifty-six cases of **general paralysis of the insane** treated with salvarsan. In 12 patients there was a marked amelioration of symptoms; 6 of these were freed from restraint, and are pursuing their ordinary work. Browning and McKenzie (Brit. Med. Jour., Sept. 23, 1911).

**Diagnostic Value of Salvarsan.**—In obscure lesions in patients presenting no evidences or history of syphilis, salvarsan may be of considerable diagnostic value, its administration causing rapid improvement if syphilis is the cause.

In tertiary and latent cases of syphilis, with conditions present suggesting neoplasm, and with the Wassermann negative, a provocative injection of salvarsan, by causing the Wassermann to become positive if the disease is syphilitic, will in many instances prove of great assistance.

**Salvarsan Treatment in Pregnant Syphilitic Women.**—Such treatment has been found very advantageous, and unattended with danger, either of abortion or to the mother's life, provided moderate doses be used. The effect on the child depends upon whether the maternal syphilis was acquired before or during pregnancy as well as the time and number of salvarsan injections, etc. If the mother's infection is treated early the chances of her giving birth to a healthy child are good, whereas if salvarsan treat-

ment is begun late in pregnancy, syphilis having been contracted some months before, the outlook is much less favorable.

Salvarsan cannot be given too early in pregnancy when symptoms of syphilitic disease are present. To prevent abortion and secure the birth of a healthy, non-specific child, the treatment should be followed by mercury and the Wassermann reaction used to note the result of the treatment. These observations reverse Colles's law, that mothers of specific children are immune if symptoms are absent. The serum test shows that such mothers are to be considered as infected. Langes (Wiener med. Klinik, Nu. 20, 1911).

A woman with secondary syphilis and in the sixth month of pregnancy was treated with 0.4 Gm. intravenously, repeated after five weeks. A healthy child was born at full time, and six months after the birth both mother and child were in good health. Browning and McKenzie (Brit. Med. Jour., Sept. 23, 1911).

Study of the effects of salvarsan administered intravenously in 10 pregnant women in doses of 0.5 Gm., and subcutaneously in 8 newborn infants in doses of 0.03 Gm. Injections of salvarsan in the dose mentioned are not without danger to the fetus, more probably owing to destruction of the treponemata than to a direct action. In about one-half the cases a pronounced weakening in the fetal heart sounds was noted in the days succeeding the injection, and in 2 cases there was some fear lest the child die in the three or four days after injection. The results yielded by the Wassermann test at a given moment in the mother and child may not correspond. Apparent maternal cure with negative serum reaction does not imply that the child is out of danger. The child of a mother in whom the first injection of salvarsan had been given five and one-half months before parturition was born healthy. A child born seventy-two

days after salvarsan injection, however, was syphilitic. One woman developed grave albuminuria nineteen days after injection, and died five days after delivery, about five weeks after the injection, of pneumonia. Only 0.2 Gm. (3 grains) had better be used for pregnant women, repeated in six days. P. Bar (Bull. de l'Acad. de Méd., Oct. 31, 1911).

A patient in the ninth month of pregnancy stated that she had had a single pimple on the external genitals when two months pregnant, and that mucous patches had appeared during the fifth month. An intravenous injection of 0.4 Gm. of salvarsan was given, and in four days the mucous patches had disappeared; the only ill effect was a slight diarrhea, which continued till her confinement, ten days later. She was delivered of a living girl weighing 4380 Gm. and showing no syphilitic lesion. The placenta weighed 860 Gm., and had the appearance of minced pork. Six months after confinement the mother showed no symptoms of syphilis, having received a second injection six weeks after confinement. The baby at fourteen months was healthy. Oui (Écho méd., March 24, 1912).

Six pregnant women and eighteen infants treated with arsenobenzol. In women acquiring syphilis or showing secondary symptoms during pregnancy one may suppose that the fetus is not yet infected and that the administration of repeated salvarsan injections, in doses of 0.25 to 0.3 Gm., is therefore clearly indicated. In cases, however, that have not recently exhibited any symptoms of syphilis, and in which the sole aim is to avoid interruption of pregnancy by premature expulsion or fetal death, mercury and iodides are to be given the preference over salvarsan. Fabre and Bourret (Lyon méd., Nov. 3, 1912).

The liver and kidney during pregnancy usually permit the elimination of the drugs without injury, yet there is always an element of uncertainty, and this is the special danger of salvarsan medication during pregnancy.

Cases have been published in which the liver and kidneys seemed to be functioning normally and yet the balance was upset so easily that salvarsan caused serious injury. Sauvage (Annales de gynéc. et d'obstét., Jan., 1913).

Antenatal treatment with arsphenamine is far superior to the early administration of thorough treatment with mercury and potassium iodide in a pregnant syphilitic mother. Not only does it seem possible to start the treatment much later, and yet be successful, but apparently salvarsan enables the mother, in the absence of further treatment, to continue to bear healthy children to the same—untreated—father. Injecting neosalvarsan intravenously in 7 pregnant women, the writer secured a healthy child in each instance. Five of the women were later pregnant once again, and 3 twice, and apparently in all instances with delivery of a healthy infant. In no case had any subsequent treatment been received, except in 1, which had irregular treatment. All the cases received mercury either by injection or by mouth, along with the arsphenamine. The author urges that all records of miscarriages and stillbirths be kept, those due to syphilis determined, and the syphilitic mothers given arsphenamine and mercury. L. Findlay (Glasgow Med. Jour., Feb., 1918).

**Salvarsan Treatment in Congenital Syphilis.**—Infantile syphilis can be favorably influenced by the administration of salvarsan to the nursing mother. Sometimes, however, the results thus obtained are harmful rather than beneficial, and in any event, subsequent direct treatment of the child, when its general condition has improved, is required. Immediate direct treatment of the syphilitic infant with salvarsan may involve some danger to its life, very probably owing to the sudden liberation of a large amount of toxins from the killed spirochetes,

and is therefore not often attempted unless the child is already in a condition such that death is expected, *e.g.*, in **pemphigus neonatorum**.

Several syphilitic infants treated with the milk of syphilitic mothers that had first received a dose of salvarsan intravenously. There was some improvement of the symptoms, but not nearly as pronounced as the author had expected. In several cases an undoubted specific rash developed after the milk had been given. Analysis showed that there were appreciable amounts of arsenic present in the milk, but probably also some endotoxins and antibodies. It would be more rational to feed such infants with the milk of cows or goats that had received a dose of salvarsan. Jesionek (Münch. med. Woch., May 30, 1911).

Action of salvarsan in 26 cases of **syphilis** in infants and young children described; 13 were under a year old. The youngest was 5 weeks old. All were fairly well developed and nourished breast-fed infants. At first the initial dose was 0.005 Gm. ( $\frac{1}{2}$  grain) per kilogram ( $2\frac{1}{4}$  pounds) of weight, but later this was increased to 0.008 Gm. ( $\frac{1}{8}$  grain) and to 0.01 Gm. ( $\frac{1}{10}$  grain) per kilogram. Wechselmann's neutral suspension was found satisfactory. Three injections were given in 1 case, two injections in each of 9 others. All but one of the injections were intramuscular. The increase in weight of the infants while under observation was fairly satisfactory. The children did not suffer from digestive disturbance as a result of salvarsan. Altogether three relapses were observed; in 2, in spite of the fact that Wassermann's reaction had become negative. The cutaneous manifestations of syphilis and those of the mucous membranes improved with wonderful rapidity. In 2 cases of **osteochondritis cubitorum** improvement was very rapid, and in 1 of them after two weeks, in the other after three, the symptoms had altogether disap-

peared. There was considerable improvement in a case of **syphilitic cerebral tumor** with **hydrocephalus** and already developing optic atrophy. Bokay (Wiener klin. Woch., Nu. 17, 1911).

Case of **congenital syphilis** in an infant treated with mercury. The Wassermann in both mother and child was positive. The mother was given 0.4 Gm. of salvarsan. Its effect on her was gratifying; she felt much better than she had for a long period. Seven days after the injection the Wassermann reaction in both parent and child was negative. No arsenic was found in the milk, examination of which showed it to be normal as regards fats and total solids. Twenty-five days after the injection the child died. Chapin (Amer. Jour. of Obstet.; Amer. Jour. of Dermat., Sept., 1911).

Report of a case showing provocation of syphilitic skin eruption in an infant through the milk of the mother treated with salvarsan; another case in which numerous efflorescences appeared where the skin had previously been normal twenty-four hours after the injection of salvarsan; a third in which a recurrent erythema multiforme and syphilitic efflorescences with the already existing exanthem followed the injection; and 2 cases in which salvarsan seemed to excite a pseudosclerosis. In the latter cases the differentiation between pseudosclerosis and a fresh infection was difficult. Oppenheim (Wiener klin. Woch., Oct. 5, 1911).

Salvarsan may prove very beneficial in the syphilitic child born at term. It acts very promptly on **pemphigus** and causes rapid disappearance of spirochetes from pemphigoid lesions. It is capable of producing prompt and lasting recovery from **hydrocephalus** of syphilitic origin. Disappearance of the phenomena of **syphilis**, even when associated with a negative Wassermann, does not imply a permanent cure. It is possible that salvarsan lowers the



resistance of the newborn infant to intercurrent infections. Only 0.01 Gm. ( $\frac{1}{50}$  grain) for newborn infants should be used, repeated twice or thrice at six-day intervals. P. Bar (Bull. de l'Acad. de Méd., Oct. 31, 1911).

In syphilitic infants salvarsan was found to overcome rapidly **pemphigus**, all mucous patches, and **chronic coryza**. Its effect in improving the general condition was, however, far less constant. In cases not presenting any syphilitic manifestations except poor general condition, salvarsan should not be used unless mercury and iodides have failed. Where it is employed, its effects are evanescent; mercury and iodides should always be given afterward and the salvarsan not repeated until acute eruptive phenomena return. The authors recommend, in infants, intramuscular injections of neosalvarsan, 0.05 Gm., not into the most fleshy part of the buttock, but into the muscles covering the external iliac fossa. The needle is introduced to the bone, then withdrawn slightly, so that its point shall lie in the muscle. Since dressings at this area in infants cannot be kept clean, the puncture is merely covered with a little cotton, dipped in collodion. Fabre and Bourret (Lyon méd., Nov. 3, 1912).

Forty children with **congenital syphilis** treated. The results observed from salvarsan and neosalvarsan intravenously were about the same. In poorly nourished children mercury should be given first, followed by salvarsan. Two pregnant mothers were treated with salvarsan and the infants showed a negative Wassermann reaction, but had some signs of latent syphilis. Dunzelmann (Zeit. f. Kinderheilk., Jan., 1913).

In children less than 6 years of age, it has been the practice to give intramuscular injections exclusively because of the difficulty attending intravenous procedure in these cases. The dose considered suitable has been

0.004 or 0.005 Gm. for each pound of the child's weight. La Féra, however, has found it not inconvenient to administer salvarsan intravenously in these little patients, exposing the vein before injecting, and considers this method the best.

With correct technique the intravenous application of salvarsan in full-term infants as well as in premature births is the method of choice. In severe infections a rather large dose should be injected, that is, not under 0.04 Gm., and such a dose, from 0.04 to 0.1 Gm., will have no detrimental effects on full-term infants. In mild cases small doses should be used. In general the injection should be repeated and should be supported by other antisymphilitic remedies. Engelmann (Zentralbl. f. Gynäk., Jan. 20, 1912).

Eight milligrams ( $\frac{1}{50}$  grain) per kilogram ( $2\frac{1}{2}$  pounds) of body weight intravenously is the maximum dose of salvarsan for infants. Where the infant is enfeebled it is better to give mercury or to begin with much smaller doses of salvarsan—3 to 5 mgm. ( $\frac{1}{20}$  or  $\frac{1}{12}$  grain) per kilogram of body weight. If there be any sepsis salvarsan should be withheld. In removing the symptoms of the disease, salvarsan is more speedy than mercury. Combination of salvarsan with mercurial treatment, however, gives the best prospects of cure. C. T. Noeggerath (Jahrb. f. Kinderheilk., Feb., 1912).

Report concerning 25 cases of **congenital syphilis**, 10 of which received salvarsan with or without mercurial treatment, while 15 were treated by the use of mercurials alone. The mercurial treatment consisted of  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.032 Gm.) of gray powder three times daily, together with inunctions of 25 per cent. blue ointment every second day. The salvarsan was given intravenously. The dose of salvarsan varied from 0.05 to 0.1 Gm. ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains). A febrile reaction was seen only three

times and was very mild. There was never any necrosis or inflammation at the site of venipuncture. Of the 10 cases treated by salvarsan 2 ended fatally; all the others were decidedly improved with the disappearance of specific symptoms. Of the 15 cases treated by mercurials alone 3 improved, 2 did not improve, and 10 terminated in death. After the injection of salvarsan the Wassermann reaction was found to be still positive in 2 out of 3 cases in which the reaction was tested and in which the clinical symptoms had disappeared. While the indirect method of giving salvarsan to the nursing mother is valuable and should be used when the mother is available, the surest method consists in giving the salvarsan to the infant. Both indirect and direct administration should be employed whenever possible. The intravenous route of administration is the best. Usually it will be found easiest to expose the vein before attempting to insert the needle. The dose should be not less than 0.01 Gm. to the kilo of body weight.

Repeated injections and supplemental treatment by mercurials may be necessary. The Wassermann reaction should be followed for a year. La Fétra (Archives of Pediatrics, Sept., 1912).

Jesionek has introduced the method of giving infants the milk of goats to which salvarsan has been administered. This does away with the transmission to the infant of spirochetal endotoxins liberated when salvarsan is given to the mother, and avoids the injury to the child sometimes produced by the latter form of treatment. Jesionek's results have been good, but the procedure he advocates is not readily available—even were cows used instead of goats—and, on the whole, direct administration of salvarsan according to the usual methods is more effective.

To investigate the influence of salvarsan in lactation, milk from a woman to whom 2 intravenous injections had been given was collected. Two specimens were found to be free from arsenic. In a second case the same results were obtained. This shows that the benefit derived by a syphilitic infant from being suckled by a mother to whom salvarsan has been administered cannot be due to the presence of salvarsan in the milk and must be explained on other grounds, such as the presence of antibodies due to the destruction of spirochetes in the mother's body. Since toxicological analyses show that a full dose of salvarsan, 0.6 Gm. (10 grains), is not completely excreted after 3 weeks, the authors are strongly of the opinion that an interval of 4 weeks should elapse between each full dose, shorter intervals giving rise to a risk of cumulative action. Wilcox and Webster (Brit. Med. Jour., Apr. 1, 1916).

Manifestations of congenital syphilis in adolescents or young adults are relatively refractory to salvarsan. Gummatous processes may be quickly healed, but interstitial keratitis is not often markedly benefited, and syphilitic nervous phenomena are rebellious.

**In Diseases Other than Syphilis.—**In **yaws (frambesia)**, due to the *Spirocheta pertenuis*, salvarsan is even more effective than in syphilis. A single injection almost invariably cures it completely.

Five hundred cases of **frambesia** treated with injections of salvarsan, 498 being cured. Of these 409 were cured with one injection, 75 with two injections, and 14 with three injections. Of the 2 cases not yet cured, both show amelioration. There was an almost entire absence of complications. Other organic arsenic compounds, such as sodium cacodylate, arsacetic, etc., have no effect on yaws,

and mercury has utterly failed as a remedy. Salvarsan is a specific for yaws, and there is no danger attending its use for this disease. Henry Alston (Brit. Med. Jour., Jan. 6, 1912).

Intramuscular injections of salvarsan given in 22 cases of yaws, with excellent results. The duration of the patients' stay in the hospital averaged twenty-five days, as against three months under other modes of treatment. But 1 case required a second injection. In 3 cases from which tissues were examined for spirochetes the latter were found to have disappeared within forty-eight hours after the injection. The stay of twenty-five days in the hospital was not necessitated by the treatment, but was due to the fact that practically all cases were infected with ankylostomiasis, and removal of these parasites was necessary as a preliminary to the treatment by salvarsan. R. P. Cochin (Jour. Trop. Med. and Hyg., Sept. 16, 1912).

The number of cases of yaws at a Trinidad hospital was reduced from 250 to 29 by the use of salvarsan. Henry Alston (Brit. Med. Jour., No. 2713, 1913).

Salvarsan is well borne by the stomach provided this organ be empty at the time of administration and that no food be taken for at least two hours after ingestion of the drug. In frambesia, at least, the therapeutic effects are the same as by the ordinary routes of introduction. Brochard (Soc. de Pathol. exot.; Presse méd., Jan. 29, 1913).

Salvarsan used with success in the treatment of frambesia among Congo natives. The lesions healed within ten days, and the joint nodosities which appear related to the disease were also favorably influenced. Mouchet and Dubois (Soc. de Pathol. exot.; Presse méd., Jan. 29, 1913).

Salvarsan used in 2 cases of *ulcus tropicum*. Each patient received an intramuscular injection of 0.5 Gm. suspended in olive oil. Complete

cure took place rapidly in both cases. Hallenberger (Arch. f. Schiffs- u. Trop.- Hyg., Aug., 1912).

Treatment carried out on 36 cases of **oriental sore** (Leishmaniosis) by intravenous injections of salvarsan. There were 31 favorable results (16 cured, 4 nearly cured, and 11 much improved); 2 appeared to be unaffected, while the 3 remaining were not heard of after treatment. The drug was dissolved in distilled water and given in a dose of 0.4 to 0.6 Gm. for an adult. Of 15 cases completely cured, healing took place in fourteen days in 6 cases, in six days in 3 cases, in eight days in 2 cases, and in ten, eleven, nineteen, and thirty days in 4 cases. Salvarsan in these doses is a specific against the protozoa causing oriental sore. The dose may be repeated in a couple of weeks if improvement is delayed. P. v. Petersen (Münch. med. Woch., Nov. 12, 1912).

**Gangosa** patients at Guam were ordinarily treated with iodine mixture, but since the introduction of salvarsan this product has been given a trial, and it seems that if employed in the early stages it will prevent extensive destruction of tissue. It should however, be supplemented by a prolonged course of mixed treatment. Kerr (U. S. Naval Bull.; N. Y. Med. Jour., May 17, 1913).

Eight cases of **rat-bite disease**, occurring in various parts of Japan, treated with salvarsan. The drug was administered at different stages of the disease and also in the febrile and afebrile periods. Except in 3 cases, a single intravenous injection sufficed to prevent all further manifestations of the disease. S. Hata (Münch. med. Woch., Bd. lix, S. 354, 1912).

In **relapsing fever**, due to the *Spirillum obermaieri*, the parasites are caused to disappear from the blood in a few hours and the fever is aborted. Recurrence occurs only in about 2 per cent. of the cases if the drug be administered intravenously.

**Report of 332 cases of relapsing fever** in Indochina treated with an intravenous injection of 0.2 Gm. of salvarsan. There followed only 6 relapses, which yielded quickly to a second injection. In 24 cases there was a return of fever on the twelfth day without reappearance of the spirilla. This disappeared in one to three days. Mouzels and Nguyễn-Xuan-Mai (Bull. de la Soc. Méd. et Chir. de l'Indochine, No. 7, 1912).

In **trypanosomiasis (sleeping sickness)** salvarsan is by no means a specific as in the two affections just referred to. The trypanosomes, after an intravenous injection, may disappear for a time, but recurrence seems practically inevitable. The drug possesses no marked advantage over the allied arsenicals, atoxyl and arsenophenyglycin, nor over antimony.

The relative toxicity of salvarsan and neosalvarsan to trypanosomes was tested by the authors. Neosalvarsan proved actively parasitocidal in dilutions up to 1 in 500,000 in half an hour. Similar experiments made with salvarsan, dissolved with the minimum amount of alkali, an amount which would not injure the parasites, showed that in a 1 in 100,000 solution the organisms were still very motile after half an hour. Neosalvarsan was thus shown to be five to ten times more actively parasitocidal than the older preparation. J. McIntosh, P. Fildes, and H. B. Parker (Lancet, July 13, 1912).

**Filariasis** may be benefited by salvarsan, the parasites being inhibited for a time and the patient's general condition improved.

Case with *Filaria sanguinis hominis*, with unilateral **chyluria**, treated by 0.6 Gm. of salvarsan administered hypodermically. The urine remained unchanged for the first twenty-four hours. During the succeeding forty-eight hours it became perfectly clear for the first time since the inception

of the complaint, seven months before. Suddenly, however, from the sixty-eighth to the seventy-second hour, it became markedly chylous and contained large numbers of seemingly dead filariæ of both embryonic and adult forms. Then turbidity ceased until at discharge only an intermittent opacity was present, and no filariæ were demonstrable. Blood-smears taken continuously for one week were all negative as to filariæ, whereas before the injection there had been no trouble in finding the filariæ in the midnight specimens. P. M. and J. T. Pilcher (Med. Record, March 11, 1911).

Warning against the use of salvarsan in bilharziasis, which has not proved at all successful in its treatment. Looss (Deut. med. Woch., Jan. 11, 1912).

In **malaria** the drug is of little value except in the tertian variety, in which an absence of parasites from the blood for some weeks may result from its use. In cases refractory to quinine, salvarsan frequently proves beneficial, not only destroying the parasites, but overcoming the resistance to quinine, so that if the latter is used when the fever reappears its action will be more evident than before (McDonagh).

When salvarsan is introduced in a single dose of 0.5 Gm. intravenously in **tertian fever**, the parasites usually disappear after from twelve to forty-eight hours. The attacks cease. In quartan fever the action of the remedy does not last, even after a dose of 0.8 Gm. In the tropical form, doses of from 0.5 to 0.8 can only produce a temporary disappearance of the ring forms from the blood. The crescent form does not disappear, although it may become temporarily modified in shape and staining properties. In some cases of tropical malaria, a so-called contrary effect was noticed. After a temporary lowering of the temperature and dimi-

nution or complete disappearance of the ring-shaped parasites from the blood, there took place a distinct turn for the worse in the patient's condition, with reappearance of rings and crescents in large numbers. Iversen and Tuschinsky (*Deut. med. Woch.*, Jan. 19, 1911).

Neosalvarsan tried in 5 cases of tertian **malaria**. The plasmodia disappear quickly, but it is a question whether this is permanent. To avoid a recurrence one should give a second injection two days after their disappearance; even a third injection may become necessary. Iversen and Tuschinsky (*Münch. med. Woch.*, July 16, 1912).

Salvarsan cures the benign tertian, but does not prevent the recurrence of malignant tertian **malaria**. The injection should be given at the beginning of the attack of fever, when the young forms predominate. In the 2 cases reported a rapid recovery was obtained in both after a single intravenous injection. In both cases a positive Wassermann was converted into a negative one by the treatment. R. Cestan and M. Pujol (*Gaz. des Hôp. Civ. et Milit.*, Nov. 12, 1912).

Salvarsan in doses of 0.3 Gm. given in 3 cases of estivoautumnal **malaria**. The estivoautumnal parasite is not destroyed by this drug, but nevertheless in 1 case it was useful in preventing relapses. V. Fusco (*Gazz. d. Osped. e d. Clin.*, Nov. 14, 1912).

In skin diseases salvarsan has been extensively tried, with varying results. In **psoriasis** and **lichen planus** the remedy is of distinct value, though not very evidently superior to arsenic in other forms. Cases of obstinate **pemphigus** have been benefited by it.

Salvarsan used in 3 cases of **psoriasis**, the dosage being 0.4 to 0.5 Gm. For a few days following injection there appeared to be some improvement, but after this the condition failed to improve. Schwabbe (*Münch. med. Woch.*, Bd. lvii, Nu. 36, 1910).

Strikingly prompt improvement from an injection of salvarsan in an intractable case of **pemphigus**. During a year and a half the skin had never been entirely free from bullæ, the number present varying from twenty or more to several hundred. Arsenic in very large doses (40 minims of the liquor potassii arsenitis three times a day) had proved of some benefit, but nothing had ever prevented the development of bullæ, nor given more than temporary relief from pain. Salvarsan (0.6 Gm.) was injected subcutaneously in the scapular region. No new bullæ developed after the first twelve hours, and the skin was practically clear at the end of six days. R. L. Sutton (*Boston Med. and Surg. Jour.*, March 9, 1911).

Two cases of **pemphigus** were very favorably influenced by salvarsan injections, while under the former treatment—quinine, Fowler's solution, zinc powder, and baths—no improvement had been visible. The dose was 0.6 Gm. given intravenously. Stümpke (*Berl. klin. Woch.*, July 1, 1912).

In **lichen ruber planus** salvarsan seemed to act as a specific. A woman, 47 years of age, who received two injections intravenously, one of 0.3 and the other ten days later of 0.4 Gm., was cured of the disease after fourteen days. Polland (*Wiener klin. Woch.*, Aug. 1, 1912).

In a case of **cancer of the tongue**, all other methods having failed, the author tried arsenobenzol, a dose of 0.5 Gm. being injected intramuscularly. In from thirty-six to forty-eight hours the pain disappeared, the ulcerations cleared, and the fetid discharge disappeared almost entirely. After ten or fifteen days these symptoms reappeared; a second injection was given six weeks later, and a third ten days after that. These later injections were both given intravenously, the dose being 0.3 Gm. each time. Although death supervened five months later from cancerous

cachexia, the pain and the discharge had not reappeared. E. Bodin (La Clinique, Feb. 17, 1912).

In **pellagra** salvarsan seems to have been useful in a certain proportion of cases.

Twenty-one cases of **pellagra** treated with salvarsan by both intramuscular and intravenous methods, and in varying amounts, collected. Most cases had a single dose, 1 had two doses, 2 were given three doses. There was an untoward result in 1 case, a profuse diarrhea following the injection. In 47.6 per cent. no improvement occurred. At least temporary improvement was observed in the remainder. The well-known dangers of administering salvarsan to patients suffering from cardiac and renal lesions contraindicate its use in many cases of **pellagra**, because of their well-known tendency to myocardial and renal degeneration. If given at all, it should be given in broken and repeated doses, and preferably by the intramuscular method. H. P. Cole and G. J. Winthrop (Jour. Amer. Med. Assoc., June 17, 1911).

Report of 27 cases of **pellagra** treated with salvarsan; of these, 20 were apparently cured, 3 were doubtful, and 4 ended fatally. The author gives each patient doses of salvarsan varying in number from five to twelve at intervals of seven to ten days. The first dose was 0.2 Gm., the second 0.4 Gm., and subsequent doses were calculated on the basis of 0.1 Gm. for every 20 pounds of the unclothed patient's weight. Both syphilis and **pellagra** should be treated by giving intravenously doses of salvarsan until no reaction follows, *i.e.*, no fever, no vomiting, and no bowel disturbance. **Pellagra** cases require twice as many doses as the syphilitic.

Of the 4 deaths after salvarsan there seemed to be some connection in 3 of them between the reaction and a subsequent cerebritis or meningitis.

There appears to be but small choice in **pellagra** between salvarsan and sodium arsenilate, except that the

latter must be given hypodermically during a period varying from eighteen months to two years. E. B. Martin (N. Y. Med. Jour., March 15, 1913).

In **scurvy** salvarsan has seemed of some value, a distinct influence being exerted on the hemorrhagic manifestations and general condition.

The bad state of nutrition in buccal **scurvy** is due largely to the condition of the gums. Several intravenous infusions, usually of 0.3 Gm., were given to 8 cases. The results were remarkable in that the lesions of the mouth usually healed within a week and that the spirilla were much diminished in number, though they never disappeared entirely. The other symptoms of the disease were not, however, influenced; so salvarsan cannot be regarded as a specific for **scurvy**. Tuschinsky and Iwaschen-gow (Münch. med. Woch., Dec. 12, 1911).

In rebellious cases of **noma** good results have been obtained.

It would seem advisable, even in the absence of positive evidence that spirochetæ are the specific organisms of **noma**, to make use of salvarsan in every case which does not immediately yield to local treatment. Nicoll (Archives of Pediatrics, Nov., 1912).

**Chorea** has been treated with salvarsan with asserted advantage.

Case of **chorea gravidarum** given an intravenous infusion of salvarsan two to three months before term. The patient was cured, no return of symptoms appearing, even after delivery. The method is to be recommended in severe cases which have resisted all other measures. Thus an interruption of pregnancy may be avoided, the efficacy of this procedure being doubtful. E. Härtel (Münch. med. Woch., Jan. 28, 1913).

Cases of **leukemia** have also been benefited temporarily or permanently.

In **pernicious anemia** the drug has proven strikingly effective in a fair proportion of cases, ineffectual in others, and harmful in a few.

Seven cases of **pernicious anemia** treated with salvarsan. One showed striking improvement, four injections of 0.3 Gm. each being given during six weeks, in which time the red cells increased from 1,760,000 to 3,350,000 and the hemoglobin from 52 per cent. to 78 per cent. During the year following the last injection the blood continued to improve, the red blood-cells increasing to 6,210,000 and the hemoglobin rising to 120 per cent. Five other patients showed more or less improvement, and in only 1 was no benefit derived. To secure the best results salvarsan should be given intramuscularly, on account of the prolonged action which results. Salvarsan will probably be found a more efficient remedy than arsenic given by the mouth, and indeed more efficient than any form of treatment which has yet been employed in pernicious anemia. Bramwell (Brit. Med. Jour., June 22, 1912).

In **pernicious anemia** the intravenous injection of salvarsan produced such an anemia that the patients in 2 out of 3 cases died within three weeks, and the third patient was not improved, though he apparently was not damaged by the treatment. Both in chorea and leukemia not only did the injection of salvarsan not cure the disease, but it did not prevent the appearance of complications. Charteris (Brit. Med. Jour., Sept. 21, 1912).

Case of a woman who had been anemic for more than a year. A blood-smear showed typical **pernicious anemia**. Salvarsan, 0.3 Gm., was injected intramuscularly. Within three days benefit was apparent, although local pain was severe for about a week. In four days the hemic murmurs had almost disappeared, and the patient was much stronger. Blood examination showed a distinct improvement, and two weeks later

the same dose was again injected; this was followed by a sharp reaction; the temperature rose to 101° F. (38.3° C.). The patient looked exceedingly ill; the pallor and hemic murmurs returned, and she developed a large patch of dry pleurisy. This condition lasted a few days, when the fever slowly subsided and uninterrupted recovery set in. E. Hobhouse (Brit. Med. Jour., Dec. 14, 1912).

Case of **pernicious anemia**, in which 0.3 Gm. of salvarsan was given intramuscularly. There was a definite increase in the number of red cells for a fortnight, when a second dose was given. Examination of the blood a week later revealed a diminution in the red cells; the treatment was therefore stopped. E. F. Maynard (Brit. Med. Jour., Jan. 11, 1913).

In a case of **Banti's disease**, with typical liver and spleen and characteristic blood-count, the author obtained a cure after a subcutaneous injection of 0.4 Gm. of salvarsan. The nodules in the liver disappeared completely and the spleen slowly returned to its normal size. The only thing remaining is a leucopenia with relative lymphocytosis. The patient, a boy 14 years old, gave a distinct history of congenital syphilis. Many cases of Banti's disease are syphilitic in origin. It is the physician's duty to perform the Wassermann reaction before turning a case of Banti's disease over to the surgeon. W. Schmidt (Münch. med. Woch., March 21, 1911).

Case of a woman, aged 30 years, with very marked anemia, marked enlargement of both liver and spleen, edema and suffering from persistent vomiting and diarrhea. The patient received three intravenous injections of 0.3 Gm. of salvarsan during a period of four weeks, and was apparently cured. Perussia (Münch. med. Woch., Bd. lix, S. 1482, 1912).

Report of the case of a man, 22 years of age, who suffered from **splenic anemia**, together with tuberculosis and malarial infection. This

patient receiving two injections of salvarsan intravenously, 0.15 and 0.4 Gm.; he progressed favorably, and the author expects a cure, having just given a third injection of 0.4 Gm. Vallardi (Münch. med. Woch., July 2, 1912):

Report of a case of **splenic anemia** in an adult, treated with salvarsan. The result was good. Every patient whose case has been diagnosed as Banti's disease should receive an antiluetic, especially salvarsan, even if the Wassermann reaction remains negative. Curschmann (Münch. med. Woch., July 2, 1912).

In **sympathetic ophthalmia** marked benefit from salvarsan has been reported.

Good results from the use of salvarsan in **sympathetic ophthalmia**, the blood count becoming normal and the eye quiet. S. H. Browning (Ophthalmoscope, Nov., 1912).

Case in which an iridectomy had been performed on an eye badly injured by iritis. Seven days later the other eye showed distinct symptoms of a commencing **sympathetic ophthalmia**. The eye operated on was enucleated at once, the patient placed in bed, and the usual treatment begun, but the eye constantly grew worse. Finally, although the Wassermann reaction was negative, 0.7 Gm. of neosalvarsan was given intravenously. Improvement began at once and proceeded to recovery. F. P. Calhoun (Amer. Jour. of Ophthalm., April, 1913).

In **small-pox** salvarsan administered early in the eruptive stage has been claimed to bring the rash to a standstill and ward off complications.

Salvarsan given in 3 cases of **small-pox**. It proved harmless and a favorable influence seemed to be exerted. Lenzmann (Med. Klinik, April 30, 1911).

By injecting 0.3 Gm. salvarsan intravenously in **plague**, the author increased the agglutinin of the serum

to five times the original amount. No destructive effect upon the plague bacilli themselves is produced. Aumann (Deut. med. Woch., Nov. 14, 1912).

In **scarlet fever** salvarsan has been tried with asserted benefit.

Salvarsan treatment given in a series of 39 cases of **scarlet fever** of severe type; 5 cases died, a mortality of 12.6 per cent. as compared with 24.5 per cent. mortality in 44 cases not treated with salvarsan. One of the fatal cases was an instance of puerperal scarlet fever following a septic abortion, death being due to sepsis. Another occurred in a 2-year-old child who had whooping-cough and died of bronchopneumonia. Two other cases when admitted suffered from severe diphtheritic and streptococcic toxemia. Only 1 of the 5 fatal cases was thought to be due to actual scarlatinal infection. The percentage of complications was much smaller in the cases treated with salvarsan. Thus, otitis media developed in only 6.6 per cent., as compared with 14.3 per cent. in the untreated cases; nephritis occurred in 25 per cent., as against 43 per cent.; and endocarditis was observed in 3 per cent., instead of 16 per cent. The effect of the remedy was marked upon the course of the disease. In all but 2 cases the temperature fell by crisis shortly after the injection. This fall was followed by a rise on the following day, but seldom to the original height of the fever. A few of the patients received a second injection of salvarsan. The doses given were 0.1 to 0.2 Gm. to infants, 0.3 Gm. to older children, and 0.5 Gm. to adults. Most of the injections were given intravenously and only were given in highly diluted form intramuscularly when intravenous injections were impossible. Klemperer and Woita (Therapie der Gegenwart, Bd. viii, S. 198, 1912).

Salvarsan used in 109 and neosalvarsan in 8 cases of **scarlet fever**. Upon the throat symptoms, especially in



the necrosing form, a strikingly favorable effect was produced. The necrotic lesions began to clear up with unexpected rapidity, this probably accounting for the small number of the cases in which otitis appeared. Sequelæ such as glandular enlargements and nephritis, on the other hand, were not warded off by the remedy. The milder cases of scarlatina do not require salvarsan treatment, which is indicated, however, in the severe toxic forms. *Neosalvarsan* is not suitable for the treatment of scarlet fever. G. Jochmann (Congress on Internal Medicine, Wiesbaden; Zentralbl. f. inn. Med., May 31, 1913).

In **anthrax**, experimental and clinical, trial of salvarsan seems to have shown it to be a remedy of some value.

Case of **anthrax** in which the prognosis, according to past experiences, seemed absolutely unfavorable. An intravenous injection of 0.6 Gm. of salvarsan was given and recovery followed. G. Becker (Deut. Zeits. f. Chir., Bd. cxii, 1911).

Experiments with salvarsan on animals infected with the **anthrax** and **erysipelas bacilli**. The good effects are due to the proved property of salvarsan, of increasing the antibodies in the animals. Bierbaum (Deut. med. Woch., Oct. 24, 1912).

Experiments with salvarsan in rabbits infected with **anthrax**. Sources of error carefully excluded. In the dose of 0.04 Gm. per kilo of animal salvarsan was found capable of saving animals otherwise doomed to succumb from virulent strains of the bacilli. While the author cannot affirm that in Becker's human case the drug saved life, he advises that in serious cases of anthrax salvarsan be given. G. Schuster (Ehrlich's "Abhandlungen über Salvarsan," Bd. iii, 1913).

Case of a man severely infected with anthrax. He had a large swelling about the size of the fist on the

right side of the throat and on it was a spot with a dark crust, surrounded by many pustules. There was also enlargement of the neighboring lymphatic glands. The pus was found to contain anthrax bacilli. Morning temperature, 100.8° F. (38.2° C.). The abscess was opened by the actual cautery. An intravenous injection of salvarsan was then given. After three hours the temperature had risen to 103.6° F. (39.7° C.), but at the end of eight hours it had dropped to 100.4° F. (38° C.). On the following morning the temperature was 97° F. (36.1° C.) and the patient's general condition much improved. The swelling was greatly diminished. After six days the infiltration of the glands and skin had disappeared and on the tenth day the crust fell off. The patient felt well after the second day. No anthrax bacilli were found in blood withdrawn by hypodermic needle. Salvarsan was the principal factor in the cure. It is to be preferred to the usual method of phenol injections around the carbuncle. Mokrzecki (Münch. med. Woch., May 20, 1913).

Finally, in **leprosy** salvarsan has been found capable of giving temporary relief in a number of cases. It is in no sense curative.

Nineteen **leprosy** patients under salvarsan treatment for eighteen months. The drug was given intravenously in doses of 0.5 to 0.6 Gm. The only ill effect following was an exacerbation of the neuritis in anesthetic cases. In 2 anesthetic cases salvarsan was unsuccessful, and except in the very early stages the drug should not be employed in this condition. But in *lepra tuberosa* the effects are very gratifying, especially in the less advanced stages of the disease. Lepromata recede in size and degenerate, and the bacilli they contain are reduced in number. In affections of the mucous membranes, especially of the larynx and pharynx, benefit is very marked. The general condition of the patient is always

greatly benefited, with a return of interest and energy. On the other hand, nervous symptoms show no change for the better, and little effect is produced on ulcers due to trophic interference. The Wassermann reaction remains unchanged throughout. J. P. Rocamora (Lepra, Sept., 1912).

In 4 leprosy patients administration of salvarsan resulted in clinical improvement. The least advanced cases showed the best results. In 1 case, *Bacillus lepra* disappeared from the nasal secretion. The patients showed partial or complete resolution of the nodules. Wellman (N. Y. Med. Jour., Nov. 16, 1912).

**Local Uses.**—Salvarsan has been applied to the throat in **Vincent's angina** with marked success.

**Vincent's angina** may be favorably affected by the use of salvarsan. The drug may be applied directly to the lesions in powder form or may be mixed with glycerin and applied on a tampon. The applications are made twice a day. In from three to five days in most cases the cure is complete. J. Anglada and P. Reveille (Progrès méd., Feb. 15, 1913).

The author recommends in severe cases of **Plaut-Vincent angina** general salvarsan treatment, together with the local application of salvarsan glycerin. J. Citron (Berl. klin. Woch., April 7, 1913).

Case of **Vincent's angina** which developed the day after a third injection of arsphenamin, contraindicating the use of this arsenical in the disease. No better result was obtained from its local application. Prompt improvement in the same case followed, however, the intravenous use of tartar emetic. Hillsman and Driscoll (Va. Med. Monthly, Aug., 1925).

It has likewise proven useful in various other non-syphilitic buccal disorders.

Report of 16 cases of **scarlet fever** in which ulcerative and gangrenous complications were particularly seri-

ous. Salvarsan was employed, generally in the form of local applications of 1:10 or 1:20 solutions in glycerin, and sometimes intravenously. The action of the drug was very prompt and marked, 7 recoveries occurring among 12 especially grave cases. In 1 case of **noma** terminating fatally, the buccopharyngeal lesions had been cured, and death was due to a gangrenous focus in the lung. Netter (Bull. et mém. de la Soc. méd. des hôp. de Paris, No. 25, 1912).

In the treatment of a case of **chronic superficial glossitis** 1½ grains (0.1 Gm.) of salvarsan were dissolved in ½ ounce (15 Gm.) of glycerin, of which quantity about a half was used in hourly swabbings over ten hours. The patient had been under careful medical treatment on and off for seven years, had given up smoking for short periods, and had improved under these treatments temporarily, but he asserted that his tongue had never been so comfortable or looked so well for ten years. At the end of one week, the ulcers had diminished to one-fourth their size. There was no history of lues. A. A. Allport (Brit. Med. Jour., Aug. 17, 1912).

Local applications of from 5 to 10 per cent. watery or glycerin solutions of salvarsan and neosalvarsan in spray form in the local spirochetoses (such as Vincent's angina, **ulitis simplex**, **stomatitis**, **noma**, and **alveolar pyorrhea**) advised. In these cases it is ordinarily a specific. The intravenous injection should be reserved for the severe cases accompanied by general symptoms. Gerber (Münch. med. Woch., March 25, 1913).

Many kinds of **ulcers** heal quickly after a single dusting with neosalvarsan or salvarsan diluted with xeroform (tribromophenol bismuth) in the proportion of 1 to 3. The after-treatment is a daily dusting with xeroform lightly sprinkled on. Water or lotion is not allowed to touch the sore. Salvarsan mixed with bismuth subnitrate was tried in 3 cases and

found satisfactory. The ulcer was protected with loosely applied lint. The surrounding skin may be painted twice with tincture of iodine. The patient is kept in bed for one day. Henry Alston (*Brit. Med. Jour.*, No. 2713, 1913).

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### DIPHTHERIA.—DEFINITION.

—Diphtheria is an acute infectious and contagious disease produced by the presence and development of the Klebs-Loeffler bacillus. As it occurs in man, it is usually characterized by the presence of false membranes upon the surfaces primarily attacked, especially the mucous membranes of the nose, pharynx, larynx, or trachea. There can no longer be any question of the specific relation between the great majority of cases of the disease known since the time of Bretonneau as diphtheria and the bacillus with which Klebs and Löffler have identified their names. The bacillus is regularly obtained in cultures from affected throats; it can readily be isolated, and when pure cultures are injected in animals they reproduce the essential features of the disease met with in man. Welch and others, by inoculating the mucous membranes of guinea-pigs, have even succeeded in producing the false membranes so closely associated with the disease in man. All the constitutional effects and characteristic lesions, except the formation of membrane of diphtheria, have likewise been produced by the injection in animals of the toxins produced by the specific bacillus. In experimental diphtheria, induced either by the injection of cultures of the Klebs-Löffler bacillus or of its toxins, the most striking feature is the production in animals of the paralyses due to nerve

and muscular degenerations, such paralyses reproducing most exactly the phenomena so often observed in clinical diphtheria. This feature of the experimental process has so impressed itself upon those most interested in laboratory researches that some propose to define diphtheria as an acute infectious disease produced by the action of the Klebs-Löffler bacillus, and characterized by the development of nerve degenerations.

While this teaching may be most in harmony with the combined evidence of clinical observation and laboratory research, it does not yet seem advisable to so far depart from the conceptions of diphtheria which have heretofore obtained. The appearance of false membrane has long been regarded as almost diagnostic; it still belongs to the great majority of cases, and can readily be appreciated, while the nerve degenerations, if they appear at all in clinical diphtheria, are met with only in the later stages of the disease, long after the question of diagnosis will have been determined.

**VARIETIES.**—The classification of the acute inflammations affecting nose, throat, etc., has not yet reached a satisfactory stage. The distinctions based upon the presence or absence of pseudomembranes have lost their significance.

While the great majority of pseudomembranous inflammations of these parts are due to the action of the diphtheria bacillus, a considerable number of such inflammations are produced by the action of other bacteria, especially the streptococci and staphylococci. On the other hand, the action of the diphtheria bacillus is not always attended by the production of pseudomembranes. The intensity of the local action of the

bacilli varies greatly, and it has been found that this diphtheria bacillus may be the cause of simple inflammatory processes, formerly designated as catarrhal, which present no appearance of false membranes. Moreover, we find that the all-important question in any case, both with reference to prognosis and treatment, is the presence or absence of the diphtheria bacillus. We, therefore, abandon the former classification into catarrhal and pseudomembranous processes and speak of:—

1. *Diphtheria*, or *true diphtheria*, in which we include all cases of acute inflammations affecting mucous membranes associated with the presence of the diphtheria bacillus in sufficient number to constitute a probable causative agent. Thus, if a culture from a sore throat shows the presence of the diphtheria bacillus, that case is at the present time accepted as diphtheria, whether there be or not pseudomembrane present, and no matter what other bacteria be associated in the culture with the diphtheria bacillus. It must, however, be noted that the presence of the diphtheria bacillus without further clinical evidence does not constitute diphtheria any more than the presence of pneumococci in the mouths of healthy persons constitutes pneumonia.

2. *Pseudodiphtheria*, in which we include all cases resembling diphtheria, but not showing the presence of the diphtheria bacillus in cultures from the affected parts. Such pseudomembranous inflammations are commonly seen as complications of the acute infectious diseases, especially scarlet fever and measles. Cultures from such cases regularly show streptococci, or staphylococci, or both. The streptococci are especially frequent. Pneumococci and other bacteria have been found.

Outbreak in a girls' school of sore throat, bacteriologically proved due to a form of Klebs-Löffler bacillus, the resulting illness, however, failing to present the typical features of classical diphtheria. It might have been termed a "diphtheritic fever," the symptoms of which were as follows: A more or less severe coryza; a moderate tonsillitis, usually one-sided, and unattended by high fever or by much exudation; thickly coated tongue and foul breath, the tongue desquamating as in scarlatina; a patchy or punctate rash on the roof of the mouth and buccal mucous membrane; swelling of the cervical lymphatic glands; a roseolar rash on the skin (in 12 out of 18 cases—in 4 cases early in the attack, in 8 cases on the fifth to the seventh day from the first symptoms or invasion); distinct desquamation (in 3 cases), the peeling being particularly marked on the hands. Moore (Dublin Jour. of Med. Sci., Jan., 1908).

The site of the diphtheritic process, whether nose, tonsils or pharynx, or larynx, materially affects the symptoms and course of the disease; we, therefore, in our description, speak of *nasal*, *pharyngeal*, or *tonsillar*, and *laryngeal diphtheria*. In the effort to further classify their cases some divide them upon the basis of the bacteriological findings in cultures from the throat. Thus, when the culture shows diphtheria bacilli practically alone, they designate the case as bacillary diphtheria; when cocci are present in considerable numbers with the diphtheria bacilli, as cocco-bacillary diphtheria, etc. This method would be highly satisfactory did the clinical course and outcome of the disease correspond to the bacteriological findings, but they do not. The presence of cocci in the cultures does not show that they will play any important part in the disease, and the complications produced by their action—such as pneumonia and nephritis—seem to be as

frequent in cases that give apparently pure cultures of the diphtheria bacillus from the throat as in those that show many cocci as well. When we have to do with a systemic infection with streptococci as well as the diphtheria bacilli, we speak of the cases as "mixed infections"; but the distinction is based upon the clinical symptoms of the disease and not upon the results of the bacteriological examination. We find it most advantageous to divide the cases into mild, severe, or septic, according to the character of the symptoms presented.

Corresponding to these three forms of diphtheria, Monti presents a classification based upon the character of the exudate in the throat:—

1. A fibrinous form, in which the diphtheritic products are only placed upon the mucous membrane, not incorporated with it. Virchow, Weigert, and Cohnheim call this the croupous form.

2. A mixed form, called also the phlegmonous form, in which the fibrinous exudate lies deep in the tissues as well as upon the mucous membrane.

3. A septic, or gangrenous, form, in which a fibrinous pseudomembrane is formed in the deep tissues of the mucous membrane, the process really consisting of a necrosis of the tissues and a mingling of the dead particles with the diphtheritic products.

Similar classifications are presented by other Continental writers; but we have not yet found it of advantage to attempt to classify our cases by the local appearances of the throat. Certainly the distinctions that Monti makes call for very nice and rather difficult discriminations.

**SYMPTOMS.**—These vary sufficiently with the site of the lesions to make it of advantage to consider the local forms separately.

**1. Nasal Diphtheria.**—Diphtheria of the nasal cavities is, in most cases, simple extension from the fauces or larynx. It may, however, occur as a primary affection. It is characterized by more or less complete obstruction of the nares, a thin, mucopurulent, and often bloody discharge from the nostrils, and a more or less marked toxemia. Pseudomembrane may be developed and may be visible through the anterior nares, but, as a rule, we see no membrane. The nasal discharge is usually very irritating, and the nares become excoriated. There is usually enlargement of the submaxillary lymphatic glands.

The degree of the toxemia varies markedly. Usually it is very moderate, the temperature is not high (100° or 101° F.—37.8° or 38.3° C.), the prostration is not marked, and the chief danger of the cases seems to lie in an extension of the process by continuity of tissue, to the pharynx or larynx, or the development of pneumonia.

The affection is often protracted, the discharge from the nose and the obstruction persisting for weeks, despite careful treatment.

Lennox Browne reported a total mortality of 63.4 per cent. in a series of cases of diphtheria involving the nose, and attributes to the nasal affection more importance than to the laryngeal. Few writers or clinicians can agree with this opinion. In practically all the cases of the series reported other parts were involved besides the nares, and the mortality record is a tribute to the gravity of extensive diphtheria rather than to the danger of the nasal affection alone. In infants, however, nasal diphtheria frequently proves fatal. It may readily

be the origin of a pharyngeal or laryngeal process. It may, furthermore, be the means of communicating the disease to others.

The writer had 92 instances of primary nasal diphtheria out of 222 cases of diphtheria. Thirty-one of the children were less than 1 year old; from 4 to 13 years of age this form was not uncommon. In the infant more than 75 per cent. of cases of diphtheria develop primarily in the nose and remain isolated in the mucosa. L. Landé (Berl. klin. Woch., Dec. 17, 1917).

The writers found diphtheria bacilli in the nose of infants more often than in the throat, a primary diphtheria of the nares being comparatively common in infants exposed to infection. It is almost invariably mild, but it may be followed by secondary diphtheria of the throat, and the mild nasal diphtheria may give rise to severe diphtheria in others. Association with streptococci renders the outlook graver. Santos (Annaes Paulistas de Med. e Cirur., Sept., 1918).

Nasal diphtheria following enucleation of the tonsils and adenoids was observed by the writer. This seems to indicate that upon removal of the tonsils infection may be diverted to a situation where it escapes prompt recognition and serum treatment, the patient then becoming a carrier. B. Seymour Jones (Brit. Med. Jour., Mar. 25, 1922).

Diphtheria bacilli not infrequently cause purulent inflammations of the sinuses. A complete cure may be obtained by antitoxin and vaccine treatment, and surgical interference is not necessary. Sonnenschein (Deut. med. Woch., Aug. 14, 1925).

The writer observed 13 cases of chronic diphtheria of the nose with symptoms of ozena. All recovered after large doses of **antitoxin** and an **autogenous vaccine** had been administered. Abraham (Deut. med. Woch., Dec. 15, 1925).

Preliminary nose and throat cultures for diphtheria bacilli should be taken

as a routine before operations such as tonsillectomy and adenoidectomy. If the cultures are positive, a prophylactic dose of 1500 units of diphtheria **antitoxin** should be injected, unless the patient has already been tested with the Schick test and shows a definite negative reaction. Zingher (Am. Jour. Dis. of Childr., Jan., 1926).

## 2. Pharyngeal, or Tonsillar, Diphtheria.—(A) *Mild Cases Without Membrane, or Catarrhal Diphtheria.*—

During the prevalence of an epidemic of diphtheria, especially in institutions, a certain number of cases may be observed in which, without the appearance of pseudomembrane, the pharynx and tonsils become reddened and somewhat swelled, the children complain of slight soreness of the throat and have a rise in temperature, but do not appear or feel very ill; yet, cultures made from such throats show the presence of the diphtheria bacillus. Such cases we have learned to class as true diphtheria. The mildness of the affection is attributed either to the small number of bacilli present, to a diminution in the virulence of the bacilli, or to an increased resistance on the part of the patient. In many of these cases the nose is involved as well as the pharynx and tonsils, and there is consequently a thin, watery, irritating discharge from the nostrils. In the course of a few days all symptoms subside, and the bacilli disappear, or they may persist for weeks without further symptoms.

The bacilli derived from cultures from such cases may prove to be fully virulent, and any such case may readily be the means of communicating a severe or virulent type of the disease to others.

The patients themselves may show albuminuria during the course of their

mild attack, or they may later develop the paralysis belonging to the severer types of diphtheria. The latter outcome is, fortunately, rare.

From the catarrhal process in the throat and nose there may arise by extension a diphtheritic laryngitis either catarrhal or pseudomembranous in character, which may be followed by stenosis or other grave symptoms.

(B) *Mild Cases, With Membrane, of Pharyngeal, or Tonsillar, Diphtheria.*—These cases are characterized by the development of more or less pseudomembrane upon the tonsils, fauces, or pharynx and a moderate toxemia. The onset of the trouble is marked by sore throat, a moderate fever, 100° or 102°, and a slight prostration.

Upon examining the pharyngeal cavity we usually find one or both tonsils reddened, swollen, and presenting upon their surfaces one or more patches of pseudomembrane. These patches may be small and difficult to distinguish from the yellow plugs seen in follicular tonsillitis. The membrane is usually firmly adherent to the underlying tissue, and, if removed, leaves a bleeding surface. The area covered by membrane may sometimes be marked off from the surrounding tissues by a zone of congestion. The membrane is usually white-gray or grayish green in color, sometimes yellow, and the patches are of irregular form. It is sometimes thick and heavy, sometimes so thin as to be translucent.

In contradistinction from this description of diphtheritic membrane we might set the characters of pseudomembrane not diphtheritic, but the more painstaking the description, the more evident would it become that it is perfectly impossible to distinguish one from the other by simple inspection.

Nothing short of a bacteriological examination will enable us to make the distinction with certainty.

With such appearances in the throat there is usually a distinct swelling and tenderness of the submaxillary and cervical lymph-nodes.

The extent of membrane in the mild cases is usually limited, and there seems little tendency toward spreading; but, on the other hand, we may see cases in which tonsils, fauces, and pharynx are covered with membrane and yet the constitutional depression is slight.

After the onset in a mild case the membrane may extend somewhat, so as to involve the fauces or pharynx; but may remain limited to the tonsils. The throat continues sore, the temperature shows some elevation, and the children feel moderately sick. In the course of three to five days the membrane begins to separate, either gradually or in masses, the throat clears up, the temperature falls, the glandular swelling subsides, and in a week or so the patient is well again.

A mild diphtheria may be accompanied by albuminuria, and may be followed by nephritis or paralysis, but, as a rule, the cause is benign and the outcome satisfactory. We must, however, be prepared at any time to see an apparently mild case of diphtheria change character and become a virulent infection. From a mild tonsillar, or pharyngeal, diphtheria a severe diphtheritic laryngitis may be developed.

The most troublesome feature of these mild cases of diphtheria is the difficulty of maintaining proper quarantine. If adults, the patients do not regard themselves sick after the first day or two, and can hardly be made to understand that, even when well, they may be the source of grave danger to others.

If the patients are children, the parents find it difficult to take a serious view of an apparently trifling sore throat, and are often unwilling to take the necessary precautions to prevent the spread of the disease. It cannot be too emphatically laid down in such cases that the clinical phenomena are no test of the virulence of the bacteria present. From an apparently mild case Park obtained the most virulent bacillus he has yet met with, and employed its toxins in the production of antitoxin of unusual strength. It has, likewise, long been well known that an apparently mild case of diphtheria may communicate a malignant infection to others.

The mild cases should be quarantined just as faithfully as the most severe, and should be allowed freedom only when the specific bacteria have disappeared from the throat.

(C) *The Severe Cases.*—In these the manner of onset may be sudden, with chill, vomiting, fever, and severe sore throat, the temperature rising to 103° to 104° F. (39.4° to 40° C.), and the prostration being marked, or the affection may begin as a mild case and gradually develop the severe symptoms, the invasion being very insidious. If seen at the beginning, there may be little membrane visible in the throat, only a small patch or two upon the tonsils, exactly similar to that described in the mild cases; the throat will, however, be more reddened and the swelling more marked. The submaxillary and cervical lymph-nodes will be swollen and tender. The child looks and acts sick. The elevation of temperature may not be in keeping with the degree of constitutional depression, oftentimes being only 101° to 102° F. (38.3° to 38.9° C.). As the disease develops, the membrane rapidly ex-

tends, until the tonsils, pharynx, uvula, and fauces are covered with a thick gray, green, or even black layer of necrotic material. If any effort be made to remove it the underlying tissues bleed freely. The membrane fills the rhinopharynx, involves the nasal cavities, and may even appear in the nares. With the involvement of the nose there is seen a thin, acrid, often bloody and foul-smelling discharge from the nostrils. The membrane may also invade the mouth and appear upon the lips. In one case seen at the Foundling Hospital, the extent of gray membrane upon the lips, cheeks, and tongue was so marked as to suggest the possibility that the child had been drinking carbolic acid. Mechanical removal of the membrane in such cases does no good whatever; it seems only to open up a fresh surface to the attack of the virulent bacilli, and the membrane is reproduced with almost marvelous rapidity. At any time the inflammatory process may involve the larynx, giving rise to laryngeal diphtheria, or it may involve the middle ear through the Eustachian tubes; in rare cases by extension through the lachrymal duct or by accidental inoculation the conjunctiva is involved.

With the increase in the local process the lymph-nodes of the neck become more swollen and tender, until it seems that they will surely suppurate, but they rarely do so. The constitutional depression becomes more and more marked. The pulse becomes more rapid and feeble; the strength fails steadily.

Two distinct types of circulatory inefficiency are encountered in diphtheria. One is always preceded by the onset of arrhythmia and has long been attributed to a state of "cardiac paralysis." In the second form a normal rhythm is maintained even in fatal cases. Cases which maintain a



normal rhythm the writer classes under the vascular type; while cases which develop a marked arrhythmia with rapid pulse and in which paroxysms of regular tachycardia may occur he places under the cardiac type. The first type—normal rhythm—are usually fatal within the first ten days of the disease, and present the appearance of profound exhaustion. The pulse remains regular, but soon becomes weak and frequently disappears entirely from the wrist. The heart, however, continues to act until within a few hours of death. E. B. Gunson (*Lancet*, Nov. 3, 1917).

Study of 242 cases of diphtheria in the Philadelphia Hospital for Contagious Diseases by the writer. Of these 72 per cent. progressed without cardiac disturbance; the other 28 per cent. exhibited such. Of the pulse abnormalities, 65 per cent. consisted of sinus arrhythmia and of sino-auricular block, both of which were probably without pathologic significance; 20 per cent. consisted of premature contractions, those of auricular origin predominating; the remaining 15 per cent. consisted of high grade heart block of sudden inception about the seventh day, which rapidly deepened into coma, death promptly resulting within 36 hours. Heart block was the only cardiac abnormality which resulted in death; in this series of cases it invariably terminated fatally. S. Calvin Smith (*Trans. Amer. Med. Assoc.; Med. Rec.*, June 18, 1921).

The temperature may not at any time be very high, 101° or 102° F. (38.3° or 38.9° C.), or it may reach 103° or 105° F. (39.4° or 40.5° C.). The swelling and tenderness of the throat render swallowing painful and sometimes almost impossible. The tonsils may almost meet in the median line; the nostrils may be plugged, and even respiration seriously interfered with. At times in the early days of the disease we may see fluids regurgitate through the

nose, when an attempt to drink is made, and it may be difficult to determine whether the regurgitation is due to the obstruction of the throat by swelled tonsils or to early paralysis of the pharyngeal muscles.

As the diphtheria advances, the urine becomes scanty and high colored, and contains albumin in some quantity; at times an acute exudative nephritis is developed, with large quantities of albumin, casts, and even blood. The onset of the complication may bring in its train, all the symptoms of an acute nephritis.

Although renal complications occur in the course of diphtheria, it is only in some few cases that they produce symptoms which cause immediate anxiety. In the large majority, they possess very little importance so far as the immediate future is concerned. N. Tirard (*Practitioner*, Jan., 1909).

Study of the blood-pressure. The maximum blood-pressure of normal children, according to Seiler, who used the Riva-Rocci instrument, is 75 to 80 mm. from 2 to 3 years; 79 to 90 mm. from 4 to 5 years. Cook and Briggs found slightly higher figures with their modification of the Riva-Rocci, and place them at 75 to 90 mm. up to 2 years, and 90 to 110 mm. after 2 years. Of the 179 cases observed by Rolleston, 63, or 35.1 per cent., according to Cook and Briggs's estimate, and 45, or 25.1 per cent., according to Seiler's figures, showed for varying periods a pressure below the normal. The varying degrees of depression bore a direct relation to the severity of the attack, being pronounced in severe and slight in mild cases. In the very severe class, of 22 cases, 18 according to Cook, and 17 according to Seiler, showed from 5 to 45 mm. below normal. The fall in pressure occurred rapidly and steeply, there being at times 10 mm. difference between the morning and evening readings. A difference of the reading of

the two wrists indicated a grave prognosis. The severe and the moderate class of cases showed a considerable fall, but less marked than in the very severe class; the severe class showing 25 and 16 cases respectively, with fall of from 3 to 24 mm., and the moderate class 11 and 6 respectively, showing a fall of from 1 to 14 mm. Rolleston (Brit. Jour. Dis. of Children, Oct., 1911).

The mind may remain clear throughout; but, as a rule, with the deepening of the toxemia the patients become dull and listless. In the severest cases stupor or delirium may be developed. Coma is rarely seen. Convulsions may occur either early or late in the disease, from the toxemia of the diphtheria or from uremia.

In some cases the patients die from the diphtheria toxemia alone; but in most of the fatal cases one or the other of the complications is the direct cause of death. Most important of these is the pneumonia. Although most often seen in laryngeal cases, pneumonia is a common sequela of diphtheria, either nasal or pharyngeal. The onset of the bronchopneumonia is usually marked by a decided rise in the temperature, a quickened respiration, and some cough. Not till the pneumonia has advanced to the consolidation of large areas do definite physical signs attest its presence. Usually we hear more or less numerous fine crackling râles over one or both chests posteriorly. Later there may be scattered areas of dullness, with bronchial voice and breathing. For evidence of the onset we must depend upon the rational rather than the physical signs. The development of pneumonia is always a grave and often a fatal complication. In but few fatal cases do we fail to find a more or less extensive involvement of the lungs, and in the

greater number it plays an important part in the unhappy outcome.

If the view at present generally held, that the complicating pneumonia is dependent upon the action of streptococci or pneumococci and not upon that of the diphtheria bacillus itself, and, therefore, antitoxin can only indirectly affect its onset or its violence, be true, then the problem of further reducing the mortality of diphtheria must depend upon the solution of the prevention and treatment of this complication. At present it is of importance to watch for signs of its onset and to be prepared to take measures to limit its extension and enable the patient to bear the attack. The most malignant cases of diphtheria die within forty-eight hours of the onset of the disease, and even in these we find more or less extensive areas of bronchopneumonia. Most of the fatal cases terminate after five or ten days, the patients being exhausted by the toxemia of the disease or the pneumonia.

In the more favorable cases improvement usually begins about the fourth or fifth day. The change is shown in both the blood and the general condition. In the throat the membrane ceases to extend and begins to separate. The separation begins upon the edge of each patch, the separated portions forming loosened tags in the nose or throat, or the membrane may come away *en masse* in the form of casts of the affected parts. The surface beneath the membrane is at first raw and bleeding, but is usually quickly covered by new epithelium. On the tonsils, however, ulcers are formed, which, healing slowly, leave irregular, depressed areas of cicatricial tissue, giving to the tonsils the excavated appearance so often seen after severe diphtheria. With the separation

of the membrane the purulent discharge from the nose and mouth gradually ceases, but a catarrhal secretion may continue for weeks afterward, such catarrhal secretion still containing virulent bacilli.

With the change in the local condition the temperature gradually falls, the pulse improves, the glandular swellings subside, the dullness or stupor disappears, and at the end of the second or third week the patient is convalescent. The patients are usually left very anemic, and the return to health is likely to be slow.

From time to time we see cases in which the formation of membrane continues for two or three weeks, the course of the disease is protracted, and recovery correspondingly delayed. In other cases the bronchopneumonia persists long after the disappearance of all evidences of the diphtheria, and may either cause death from exhaustion or may slowly resolve.

**3. Cases of Mixed Infection, or Septic Diphtheria.**—Under this head are grouped those cases in which bacteriological investigation shows the presence of the diphtheria bacillus, together with other pathogenic bacteria, usually streptococci, in some cases pneumococci, and in which these additional organisms seem to exert a definite influence upon the course of the disease. Most of these cases are fatal, and in post-mortem examinations systemic infection with streptococci or pneumococci is said to be found. The appearance of the membrane in these cases does not differ essentially from that seen in the severer forms of infection with the diphtheria bacillus alone. It may be white, yellow, gray, or olive colored, or where hemorrhages accompany the inflammatory process more or less black. The mem-

brane is usually extensive, covering the tonsils, pharynx, fauces, and uvula. The swelling of the affected parts is usually very marked, the edema being pronounced, the tonsils often so filling the throat as to preclude examination of the pharynx and giving rise to dysphagia and dyspnea. There is the same mucopurulent or bloody discharge from the nose and mouth; the nares are obstructed and the patients often breathe only through the mouth. A peculiar sickening, sweetish fector is characteristic. The lymphatic nodes and cellular tissues of the neck are most commonly swelled and indurated, the process in many cases leading on to suppuration and occasionally to gangrene. The pressure upon the veins of the neck may produce congestion of the head and swelling of the face. The swelled, dusky features, with the sanious discharge from nose and mouth, is characteristic and impressive.

The constitutional symptoms are those of a profound septicemia. The temperature often runs as high as 104° or 106° F. (40° or 41.1° C.), but may not be remarkable. The pulse is rapid, feeble, and compressible. With the feebleness of the pulse, the extremities may be cold and pale, in marked contrast to the dusky face.

Vomiting and diarrhea are common, and may be persistent. The urine contains considerable albumin and casts, and in some cases blood. The quantity may be diminished; suppression may occur and cause death from uremia. Edema of feet or hands may be seen. The liver and spleen may both be enlarged. The cerebral symptoms are marked. The patients are usually dull and stupid, indifferent to their condition or surroundings, but at times they are delirious and extremely restless,

tossing continually from side to side or crying out as though in pain. Bronchopneumonia is very common and usually hastens death. At any time during the course of the disease the larynx may be involved by extension. The cases, as a rule, terminate fatally within a week, sometimes within forty-eight hours. Rapid failure in the strength of the heart marks the fatal progress of the disease, and the end may be brought about by sudden and unexpected syncope. If they survive the first violence of the infection, these cases are especially liable to complications attributed to the pathogenic action of the streptococci, such as suppuration of the cervical lymph-nodes and cellular tissues, bronchopneumonia, and nephritis.

**4. Laryngeal Diphtheria.**—The clinical picture of laryngeal diphtheria does not present such variety as is seen in diphtheria of the pharynx and tonsils. The local effects, due to the anatomical form of structure of the larynx and its physiological function, predominate over the constitutional symptoms. The mucous membrane of the larynx possesses but little absorptive power; so that as long as the diphtheritic process is limited to the larynx the toxemia is slight.

From what has been already said it is evident that we may have laryngeal diphtheria:—

1. As a primary affection.
2. As an extension of a process beginning either in the nose or the throat.

It may also occur:—

3. As a complication of other infectious diseases, especially measles or scarlet fever. In the latter relation it is less common than the pseudomembranous laryngitis produced by the action of staphylococci or streptococci (pseudodiphtheria), and occurring as a complication it presents itself in one of the

two preceding ways, either primarily or secondarily to diphtheria of the nose or throat.

Diphtheria of the larynx begins gradually with a hoarse cough and voice, and perhaps a slight stridor with inspiration. The temperature is usually low,—99° to 101° F. (37.2° to 38.3° C.),—and the child does not appear very sick. The early stages are not to be clinically distinguished from acute catarrhal laryngitis, except that the onset of the latter is usually more abrupt and the temperature higher—102° to 103° F. (38.9° to 39.4° C.). The course of diphtheritic laryngitis has the following rather characteristic sequence of symptoms: Croupy cough, croupy inspiration, aphonia, stridulous expiration, suprasternal and infrasternal recessions, restlessness and jactitation, and cyanosis. The cough becomes more and more hoarse; the voice, at first hoarse, fails steadily until the aphonia becomes complete; the stridor, at first only affecting inspiration, shows itself with expiration and becomes louder. With the increase in the local symptoms the temperature may continue low or may mount step by step to 104° F. (40° C.) or more. At the end of the first or second day, sometimes within twelve hours, the symptoms of laryngeal stenosis become well developed. The voice is sunk to a whisper or lost altogether, the cough is very hoarse and short (tight), there is loud stridor with both inspiration and expiration, and every effort to fill the chest grows slower and more labored. With each inspiration there is more or less marked depression of the suprasternal and supraclavicular spaces and the epigastrium. The finger-tips are blue, the lips livid, the face pale, the forehead and

perhaps the whole body bathed in perspiration as the child struggles to overcome the increasing obstruction to respiration. The perfect clearness of mind is in marked contrast to the dullness or stupor usually seen in severe types of diphtheria elsewhere. As the agony increases, the child sits up, supporting the shoulders by the arms to give free play to all the accessory muscles of respiration, or, wild with fear, throws himself from side to side or up and down in a vain effort to shake off the tightening grip upon his larynx. It cannot be too strongly laid down that the laryngeal stenosis seen in these cases is largely the result of spasm of the laryngeal muscles excited reflexly by the inflammatory process and in small part the result of mechanical obstruction by membrane or the swelling and edema that accompany it. Often we see fatal cases of laryngeal diphtheria in which the stenosis has required operative treatment, showing only a fine granular membrane, the lumen of the larynx still wide. How much swelling and edema may disappear at the time of death we cannot say, but certainly membrane alone rarely obstructs the larynx. This view is strengthened by the common experience that any excitement greatly intensifies the severity of the stenosis. A child may sleep quite comfortably though breathing stridulously and with some labor; waken it and with the first frightened cry the larynx closes as though in a vice, and, unless the child be quickly quieted, operative relief will soon be required. This point is dwelt upon at such length for the purpose of enforcing its consideration in treatment. Quiet will do a great deal in controlling advancing stenosis. Vomiting will, for a time, relax the spasm, but in true diphtheria the stenosis rapidly returns. At

any time the severity of the stenosis may relax, the symptoms all gradually subside, and the patient go on to make a good recovery, but, unless relieved by treatment, the cases usually end in death by suffocation. In such a case the cyanosis deepens, the respiration becomes more and more labored, the violent struggles for air cease, the patients sink into stupor, convulsions develop, and death soon follows.

Such an outcome is most common in infants, who usually succumb in from twenty-four to forty-eight hours from the onset. In other cases the course is slower; the disease reaches its height in from two to three days and terminates within a week.

Bronchopneumonia is a common complication of laryngeal diphtheria. It may develop as the result of direct extension of the membrane from the larynx to the trachea and bronchi, or it may result from the inspiration of the inflammatory exudate containing pathogenic bacteria. The mode of its development cannot be clinically determined. Its presence is indicated by heightened temperature, more rapid respiration, greater cyanosis, usually numerous coarse or subcrepitant râles over both chests posteriorly, and more marked prostration. It makes the prognosis much more grave in any case and frequently causes death when the stenosis has been relieved by operation. It was one of the late Dr. O'Dwyer's observations that, in descending diphtheria, when the membrane passed from the trachea into the median bronchi, this invasion of a new territory was marked by a rapid rise of temperature, which, in turn, was soon followed by developing pneumonia.

Case of diphtheria in a boy aged  $6\frac{1}{2}$  years in which a thick gush of blood

poured out of the tracheotomy wound, death taking place in eight seconds. At the autopsy there were found: erosion of the common carotid at its origin by an abscess cavity which communicated with the trachea; deep ulceration of larynx, superficial ulceration of trachea, aspiration of blood and pus into lungs; perforation of subpleural abscess of left upper lobe with circumscribed fibrinopurulent pleurisy; subacute nephritis, edema, and cloudy swelling of liver. Erosion of the cervical vessels has been recorded in scarlet fever, but never before in diphtheria. O. Lukinger (*Brit. Jour. Child. Dis.*, Aug., 1911).

When laryngeal diphtheria develops secondarily to diphtheria of the nose or throat, or as a complication of the infectious diseases, the symptoms above described are superadded to those of the original affection, and the patient is all the less likely to survive.

**COMPLICATIONS AND SEQUELÆ.**—Otitis media is an occasional complication of diphtheria. It is developed by direct extension of the inflammatory process through the Eustachian tubes and belongs to cases in which the rhinopharynx is involved in the diphtheritic process.

In some cases the ear affection is of the severest type and there is considerable destruction of the drum membrane. It may even result in gangrene.

Otitic diphtheria apparently is spread through the blood rather than directly from the pharyngeal space. Purulence may be the only clinical evidence of diphtheria of the middle ear. Routine bacteriologic examinations should be made of all ear discharges. This applies equally to mastoid operations. Diphtheria is less destructive to the middle ear than is scarlet fever or measles. Diphtheria of the ear occurs as a symptom of the general infection. Drury (*Arch. of Otolaryng.*, Feb., 1925).

Pneumonia, as stated, is the most frequent and dangerous complication. It is most common in laryngeal diphtheria, but may follow any form of the disease. It is attributed to the action of the pyogenic cocci, especially the streptococci and the pneumococcus, though Stephens and Kanthack, Wright, More, and others have demonstrated the presence of the diphtheria bacillus in the lungs.

Case of a girl, aged 4 years, who progressed favorably until after a fortnight's residence in hospital, when she became moderately feverish and very restless, and presented signs and symptoms pointing to pulmonary trouble. Alteration of the respiratory murmur was made out over the right upper lobe, though from the increasing restlessness examination was difficult. The child grew very rapidly worse, with increasing lividity, restlessness, and respiratory embarrassment. Death took place within twenty-four hours of the first appearance of symptoms. At post-mortem examination a large infarction implicating the upper right lobe was found. D. Stewart (*Lancet*, March 30, 1912).

The affection takes the form of bronchopneumonia and is commonly met with in the lower lobes, but may be seen in any part of the lungs. The areas are scattered and separate or may merge into one another till considerable portions of both lungs are consolidated. This complication usually develops at the height of the disease, but may occur at the very beginning, within the first twenty-four hours, or may arise during convalescence after the throat is clear. Its onset is marked by increased temperature, disturbance of the respiration-pulse ratio,—namely, from a relation of 1 to 4 to 1 to 3,—greater prostration, and the signs of a diffuse bronchitis; only when considerable areas are involved do we obtain the signs of con-

solidation. Lobar pneumonia may occur (0.7 per cent. of cases—Rolleston) and run the clinical course of this disease.

Pleurisy is rarely met with. Empyema may develop, especially in septic cases. Emphysema is frequently seen in laryngeal cases; it may be interstitial and may extend to the cellular tissues of the neck, but is commonly vesicular.

The heart is more seriously affected in diphtheria than in any other acute infectious disease, and many of the fatal cases are due to rapid or sudden heart-failure. This follows tonsillar or pharyngeal diphtheria frequently, and is rare after other forms. Goodall, in a study of these cases, gives three types of the affection:—

1. Heart-failure while the exudate is still present in the throat and before other symptoms of paralysis present themselves. It is then due to the direct action of the diphtheria toxins upon the nerve mechanism of the heart.

2. Heart-failure after the disappearance of membrane, but during the time of other symptoms of paralysis, when it may be due either to disturbed innervation or to fatty changes in the heart muscle, such as are met with in other fevers.

3. Heart-failure during convalescence, some time after the disappearance of membrane; it is then probably caused by degeneration of the heart muscle or of the pneumogastric nerve (neuritis).

The writer divides the pulse abnormalities into an *initial tachycardia* and the *irregularities of convalescence*. The former attends the appearance of membrane and usually subsides within 48 hours after antitoxin. All survived. It is serious only when it persists during convalescence, and is then the probable precursor of heart-block. The irregularities of convalescence arise between the 6th and 8th day of convalescence

in 28 per cent. of all cases. They comprise sinus arrhythmia and sino-auricular block, 65 per cent.; premature contractions, 20 per cent., and high grade heart-block, 15 per cent. S. Calvin Smith (Jour. Amer. Med. Assoc., Sept. 3, 1921).

In 568 cases, the writer observed clinical signs of *acute myocarditis* in 17 per cent. of the whole number and in 75 per cent. of the 118 grave cases. The disturbances of rhythm comprised an early type, generally appearing on the 8th day of illness, starting as organic heart-block, and invariably fatal, and a late type, consisting of *extrasystoles*, appearing, on an average, on the 33d day. These extrasystoles occurred in 14 per cent. of the 563 patients who survived the acute stage and in 61 per cent. of the grave cases. Of the patients with symptoms of myocarditis, 81 per cent. had extrasystoles during convalescence; none of these died of heart-failure. Schwensen (Jour. of Inf. Dis., Mar., 1922).

Whether occurring early or late in the disease, the symptoms of involvement of the heart are, in general, the same: The pulse becomes either more rapid or more often slower; it may be intermittent or irregular; in any case it is much weaker. The patients are greatly prostrated, may refuse food, and may vomit repeatedly. The surface of the face and extremities may be pale and cold, or there may be dyspnea without cyanosis. There may be some precordial distress. After continuing in this condition for hours or days the patients may rally, the heart gradually resume its normal action, the symptoms disappear, and recovery ensue. More often the alarming symptoms grow worse and the patients succumb to the cardiac weakness. Death may be caused by sudden syncope induced by slight exertion or excitement. In some of the cases the patients are regarded as thoroughly convalescent, and may be up and about when sudden and

unforeseen paralysis of the heart results in instant death. The cardiac affection, while most often seen after severe diphtheria, may be a sequela of the mildest cases. Severe and persistent vomiting during convalescence is always suggestive of impending heart-failure. Hemorrhages into the skin or from mucous membranes may be met with during the height of the disease. They are most frequent from the nose and may be so severe as to require plugging of the posterior nares. They may occur from other mucous membranes: the stomach, intestines, or rarely the bladder. In the skin the hemorrhage may give rise to petechiæ or may infiltrate considerable areas.

The petechiæ are most often seen upon the abdomen and lower extremities, but may occur upon any part of the body. They are caused by changes in either the blood or the vessels or both, and are usually seen in the severer types of toxemia. The hemorrhages are in some cases sufficient to seriously exhaust the patient, and may even cause death. Exanthems, which may be morbilliform, scarlatinal, or urticarial, may appear, unassociated with the use of serum.

But 4 cases have been published in which diphtheria bacilli were found in ulcerations around the anus. In 2 personal cases anal and vulvar lesions were primary. Mondolfo (Riv. Critica di Clin. Med., Jan. 26, 1918).

Thrombosis and embolism are among the rarer complications of diphtheria. They may affect the extremities, giving rise to the usual symptoms: sudden pain, numbness, and coldness of the limbs, followed by paralysis, edema, and even gangrene. Some of the cases of cardiac paralysis may be caused by thrombosis or embolism of the vessels of the heart. Affecting the cerebral

arteries, thrombosis, embolism, or hemorrhage may give rise to hemiplegia.

In very rare cases the stomach may be involved in the diphtheritic process; but, apart from such involvement, gastric symptoms are common.

Case of a boy, aged 2 years and 4 months, who was admitted to hospital on the eleventh day of disease and died in seven hours. At the *post mortem*, among other findings, the middle third of the esophagus presented some infection of the mucosa, and in the lower third "were two longitudinal areas of necrosis, 3.5 c.m. each in length, coalescing below, where each measured 2.2 c.m. in width, and stopping just short of the lower end of the esophagus. No diphtheritic membrane was left, but direct smears and cultures showed numerous diphtheria bacilli." It is rare to find the esophagus involved; the writer found that 22 cases had been recorded since the discovery of the bacillus. J. D. Rolleston (Brit. Jour. of Dis. of Children, Jan., 1912).

Persistent vomiting is a frequent and grave occurrence in severe cases. It may be due to the fever and toxemia, or to nephritis, or to heart-failure.

Besides the familiar complications such as cardiac failure, paralysis of the diaphragm, suppression of urine, bronchopneumonia, and certain nervous sequelæ, others may occur. The first of these is enlargement of the liver, usually associated with cardiac failure, and due to distention of the liver capillaries with blood. If recovery occurs the liver usually returns to its normal size. Disease of the arteries is also a complication, yellow patches being found in the aorta, and in the mitral valve, and nodules of varying size in the smaller arteries, especially in those of the brain. They are supposed to be due to septic micro-organisms, which are associated with the diphtheria toxins. Interlobular emphysema may occur, the air which has escaped from the alveoli of the lung appearing beneath the pleura.



It may result in pneumothorax. Clubbing of the fingers is a rare complication, and has been occasionally seen in children with whom gangrene of the lung has developed. T. Fisher (Pract., Oct., 1907).

Diarrhea is often met with during the height of the disease, and may persist for some time after the diphtheria itself is improved. It may be due to enterocolitis or may be dependent upon the constitutional condition, especially in the septic cases. The local lesions are not severe and have no direct relation to the diphtheritic process. As already noted, hemorrhages may occur from either stomach or intestine in rare cases.

The kidneys are more or less affected in all severe cases of diphtheria. The lesion may be an acute degeneration, marked by more or less albumin in the urine, or acute exudative nephritis with albumin and casts, but without dropsy or uremic symptoms. Very rarely an acute diffuse nephritis with diminished urine containing albumin and casts, or suppression of the urine, dropsy, and uremia may be seen.

The albuminuria usually comes on during the height of the disease, continues for a time, and disappears rapidly with improvement in the local symptoms. Only in the rare cases in which acute diffuse nephritis develops are the renal complications likely to persist. Marked albuminuria is always an evidence of a grave infection, while not of itself a serious complication. It is most common in the septic cases, and belongs distinctly to pharyngeal, or tonsillar, diphtheria. In very rare cases there may be hemorrhages from the kidneys.

To 41 cases of puerperal infection with diphtheria bacilli on record, the writer adds one. The false membranes develop at the site of lacerations or other lesions. Edema of the external

genitals is an important symptom when present, as in his case, and swelling of the regional lymph-nodes was pronounced in a number of cases, generally bilateral. This enlargement of the glands was an early sign. Paralysis of the sphincters was observed in some cases. The fever usually corresponds with the severity of the membrane production, but in 2 cases the temperature remained normal. In some the fever was the first sign. Prostration and somnolency were extreme in some cases; headache was another symptom. There was also great difficulty in breathing, but no wheezing or croupiness. Bourret (Obstétrique, October, 1911).

The writer observed a small epidemic of *puerperal fever* of diphtheritic origin. In his own service, 9 newborn infants developed diphtheritic coryza, and all died but 1, in spite of antitoxin treatment. He then injected every infant at birth with 5 c.c. of antitoxin, and the epidemic ceased. Brindeau (Bull. de l'Acad. de méd., Oct. 18, 1921).

Mention has already been made of the fact that, pathologically and experimentally, the most characteristic lesion of diphtheria is that affecting the nervous system and giving rise to paralysis of various groups of muscles. Clinically, paralysis is infrequent, but in its distribution, type, and course none the less characteristic. In 2448 cases collected by Sanné paralysis was noted in 11 per cent.; in a series of 1000 cases reported by Lennox Browne, in 14 per cent.; in 1071 cases belonging to preantitoxin days studied by Goodall, after deducting a mortality of 33.8 per cent., he says he observed paralysis in 125 of the 709 survivors,—17.6 per cent. of the latter number, or 11.7 per cent. of the whole number; in 3384 cases treated by antitoxin comprised in the Report of American Pediatric Society paralysis was met with in 328 cases,—9.7 per cent. of the whole number. Of the 2934 cases

that recovered, 276—or 9.4 per cent.—showed paralysis, while, of the 450 fatal cases, paralysis was observed in 52, or 11.4 per cent. Simply taking the totals of these figures without relation to the question of treatment, we have 852 cases of paralysis occurring among 7903 cases, or in 10.7 per cent.

Paralysis usually complicates the severer cases of pharyngeal diphtheria, but may be seen after milder forms, and it has even been reported as following affections of the throat so mild as to have attracted little or no attention.

Diphtheritic paralysis is sometimes associated with a diffuse but rather superficial process affecting nearly the whole of the spinal cord, followed by return of the affected structures to normal. In 2 cases of paralysis occurring 3 months after diphtheria, there were symmetrical zones of anesthesia on the hands and feet. There were also disturbances of speech, swallowing, and accommodation, with paresis of the arms and legs. Marie and Mathieu (Bull. Soc. méd. des hôp. de Paris, Dec. 8, 1921).

The time of the onset of paralytic symptoms varies greatly in different cases. It may occur at the height of the disease, in the latter days of the first week or the beginning of the second, but is usually seen some time after the throat is altogether clear during the third or fourth week of the disease, and may occur as late as the tenth week after the onset. In the cases reported by Goodall the paralysis was observed from the seventh to the forty-ninth day.

A girl of  $3\frac{1}{2}$  years with membrane on the tonsils and pillars but *negative* cultures was given 3000 units of antitoxin on the 3d day, the throat at once beginning to improve. A month later, bilateral ptosis, internal strabismus of the right eye, drooling, and paralysis of the limbs developed, followed by death from respiratory paralysis. Any throat

membrane may be diphtheritic, and antitoxin should be given without waiting for culture results. Terrell and Hallock (Med. Jour. and Rec., Apr. 29, 1924).

In 171 cases of diphtheritic paralysis collected by Ross the following distribution was observed: Palate affected in 128; eyes in 77, in 54 of which the muscles of accommodation suffered; lower extremities in 113; upper extremities in 60; trunk or neck in 58; muscles of respiration, 33. Of the 328 cases reported to the American Pediatric Society the distribution was specified in 187. Of this number, in 120 it involved the throat (palate, pharynx, and larynx); in 14 the extremities; in 11 the eyes; in 32 the heart; in 1 the muscles of respiration; in 1 the sternomastoid, while in 8 the paralysis was general.

In the series published by Goodall, the palate alone was first affected in 66 per cent. of the 125 cases, and in combination with other muscles it was involved in 12 per cent. more. In a little over one-half of the cases the paralysis was limited, and in 12 per cent. it was generalized. The affection of the throat is, therefore, much the most common. It may occur alone or be followed by paralysis of other parts: the eye, the extremities, the trunk, or neck. In some cases it precedes the cardiac paralysis, but, as a rule, the latter appears unannounced. Absence of the patellar reflexes is observed in most cases of diphtheritic paralysis, even when there is no loss of power or sensation in the lower extremities, and is regarded as a sign of the probable appearance of paralysis elsewhere.

Of 1313 patients seen by the writer, 85, or about 6 per cent., became paralyzed. Of these 85 patients, 65, or 77 per cent., recovered and 20 to 23 per cent. died.

In no one case could death be attributed solely or directly to paralysis, although in all cases it was contributory. In 10 of the cases that terminated fatally the disease was of the malignant type, while in the others it was of a severe character. Eight had nasal implication, 7 a combination of faucial and laryngeal diphtheria with tracheotomy in three instances, and 27 had greatly enlarged cervical glands. Of the latter, 2 went on to suppuration. Of the 85 patients, 53, or almost two-thirds had paralysis of the palate alone; 15 of the eyes and palate; 3 of the eyes alone (strabismus). Of the 15 who were afflicted with paralysis of the eyes and palate combined, 3 had paralysis of accommodation as well as strabismus. Paralysis of the ocular muscles alone is uncommon, and only 2 of the 68 patients recorded were affected in that way. A. Love (Glasgow Med. Jour., Oct., 1911).

The incidence of postdiphtheritic diaphragmatic paralysis was 8 per cent. in 4259 cases of diphtheria. The average date of onset of the paralysis was 39½ days after the onset of the disease. Death usually occurred within 48 hours. No drug treatment availed. Marriott had reported a case in which **artificial respiration** had resulted in tiding the child over. The writer reported 8 cases, stating that the prognosis was 100 per cent. fatal. In view of this fact treatment by means of **intratracheal insufflation**, the **pulmotor**, and the **Erlanger-Gessel apparatus** was worthy of trial. Mixsell and Giddings (Trans. Amer. Med. Assoc.; Med. Rec., June 25, 1921).

In most of the throat cases the uvula and soft palate alone are involved. Nasal voice and regurgitation of fluid through the nose evidence the loss of power in these parts, and upon inspection we see the uvula hanging straight downward, relaxed, and motionless upon the back of the tongue. Sensation as well as motion is gone, and there will be no response to irritation. If the pharyngeal muscles are involved, there is difficulty in swallowing, and, if the larynx

suffers, there will be aphonia and severe coughing upon attempt at swallowing anything by reason of the entrance of food or drink into the imperfectly closed organ. The latter class of cases is very likely to prove fatal through the development of pneumonia from the inspiration of foreign material. In the extremities—arms, legs, or neck—we see more or less complete loss of power and sensation. The paralysis may not, however, be generalized in these parts, but appears at times to attack only the muscles supplied by a particular nerve-trunk, or even a branch of a main nerve. The paralysis may be so extensive as to render the patient perfectly helpless. When the trunk is involved, the gravest danger arises from implication of the muscles of respiration. Usually the diaphragm is first involved, but the intercostals may suffer. If the diaphragm is paralyzed, the respiration is entirely thoracic; if the intercostals, then the diaphragm alone must do the work. Either affection is characterized by attacks of urgent dyspnea, with cyanosis. The mind being perfectly clear and respiration maintained only by the greatest effort on the part of the victim, the distress is often terrible. The danger of suffocation is imminent. Such an attack may pass off and there be no return; but more often they recur in a short time. The patient may remain in this condition for several days, before death finally ends the struggle.

Few of these cases recover: only 8 in 33 of Ross's series. At any time there may be involvement of the pneumogastric nerves as well as the phrenic, the new invasion declaring itself by attacks of abdominal pain, vomiting, and feeble and slow or irregular pulse. At other times the heart may continue to act normally despite the respiratory distress.

We have already spoken of the purely cardiac type of this affection, for it is impossible on clinical grounds to separate from one another the cardiac failure due to changes in the myocardium from that produced by involvement of the pneumogastric or other cardiac nerves by the neuritis. Furthermore, the two conditions are often associated. It may be well again to point out the suddenness with which cardiac paralysis may occur by quoting from the Report of the American Pediatric Society the following paragraph: "Observations of some of the individual cases are interesting, particularly those of cardiac paralysis. It is twice stated that the child had gotten up and walked out of the house, where it was found dead.

"Twice death occurred after sitting up suddenly; once, on jumping from one bed to another. One patient of 20 years got up contrary to orders and died soon afterward. Another patient was apparently well, until he indulged in a large quantity of cake and candy, soon after which cardiac symptoms developed and he died shortly."

When the eyes are affected there is indistinctness of vision, usually resulting in inability to read, caused by paralysis of the muscles of accommodation. The pupils may be dilated or sluggish in action from involvement of the sphincter iridis. Strabismus or ptosis from paralysis of the extrinsic muscles of the eyes is rarely seen.

Facial and glossal paralyses have both been reported, and in some of the severest types of general paralysis the sphincters of the bladder and rectum are said to have been involved.

If the case does not result fatally, either directly from the paralysis or from the diphtheria itself or other com-

plications, the paralysis will surely recover. In none of the cases observed by Goodall was the paralysis permanent. The time required depends upon the degree and extent of the paralysis. Those in which the throat alone is affected usually recover completely within a week or two. Cases of multiple or generalized paralysis may require three or four months to regain normal power.

Relapses occur in a little more than 1 per cent. of all cases of diphtheria. They are less frequent than late tonsillitis in convalescence from diphtheria. They do not occur before the third week. The frequency of serum rashes after reinjection is much greater, their appearance is earlier and their phenomena are more intense than usual. Relapses must be distinguished from angina redux, scarlet fever and late tonsillitis. They are usually milder than the primary attack. Comparatively small doses of **antitoxin** should be employed in the treatment of relapses. Rolleston (Brit. Jour. of Dis. of Children, Aug., 1907).

#### DIFFERENTIAL DIAGNOSIS.

—The bacteriological investigations inspired by the identification of the Klebs-Löffler bacillus have greatly simplified the question of the relationship of the various pseudomembranous inflammations.

We now know definitely that there are but two great types: the one termed pseudodiphtheria, produced by streptococci or staphylococci and belonging to the acute infectious diseases,—measles or scarlet fever,—and true diphtheria, produced by the specific bacillus, and usually a primary and independent affection.

On the other hand, these investigations have added complexity to the problem of diagnosis of throat affections by showing the presence of the specific bacilli of diphtheria in many

cases of sore throat free from membrane and previously passed over as simply "catarrhal" sore throat, and also in many of the cases of a fairly definite clinical type, formerly classified as follicular tonsillitis.

In the shifting of the lines that has followed these revelations a considerable degree of mental confusion has been engendered and an uncertainty fostered that has led many to lose all faith in the results of clinical observations. If it is necessary to rearrange the lines of classification somewhat, it is not required that we abandon all our former conceptions or no longer trust to careful observation. In the great majority of cases thorough examination and careful consideration of all the factors concerned will enable one to reach a positive diagnosis without awaiting the results of a bacteriological examination, although the latter should always be employed if possible. For the sake of clearness we shall follow the order adopted in the description of clinical symptoms.

Schick described in 1913 a method known as the **Schick test**, by which we find out the susceptibility of an individual to diphtheria: He injects a small amount of diphtheria toxin ( $\frac{1}{10}$  of the minimum lethal dose for a guinea-pig weighing 300 grams). This is so diluted that it is contained in 0.1 c.c. of fluid. This should be injected with a very small needle, taking care that it goes directly into the skin, the flexor surface of the forearm being the chosen locality. A small, raised, white-looking spot should result. Within 24 hours these areas become somewhat cyanotic, slightly edematous and reddened. In 48 hours this passes off and a brownish pigmentation follows. This reaction occurs only in persons without natural antitoxin in their blood, and if such a reaction is positive, it indicates that less than  $\frac{1}{10}$  of a unit of antitoxin is contained in 1 mil of blood, and the person may be

considered susceptible to diphtheria. Children sick with diphtheria give the reaction when tested before having received the antitoxin serum. The newly born rarely give the reaction; they are usually immune (93 per cent.). According to Zingher (*Amer. Jour. of Dis. of Child.*, Apr., 1916) from 17 to 32 per cent. between the ages of 2 and 16 years give a positive reaction.

Summarizing their results, W. H. Park and A. Zingher (*Trans. Amer. Assoc. of Immunol.*; *Jour. Amer. Med. Assoc.*, July 8, 1916) conclude that it is advisable to immunize children soon after the first year of life, giving protection at a time when the disease is most dangerous. In addition, such children show only mild local and constitutional symptoms after the injections. An immune child population could thus be developed, and the bacillus carrier would probably soon disappear.

Koplik and Unger (*Jour. Amer. Med. Assoc.*, Apr. 15, 1916) have devised a needle, bent to an angle of  $170^\circ$  one-quarter inch from its point, and mounted so as to leave exposed only the portion distal to the bend. This needle, when dipped into pure diphtheria toxin, and immediately thrust endodermally, carries with it an almost immeasurable amount of fluid—about 0.00014 c.c. Parallel observations were made with this simplified technique and the accepted Schick technique, and with perfect concordance as result. Traumatic pseudopositive reactions were entirely absent, and three-quarters of the pseudopositive reactions were eliminated.

EDITORS.

In nearly all cases in negroes examined by the writer, the pigment was darker in color than the skin. The reaction is equally as clearcut in negroes as it is in whites. Wright (*Jour. of Infect. Dis.*, Sept., 1917).

Experience of over 2500 tests on as many recruits showed that the pseudoreactions are much more frequent among adults. Much of the confusion and uncertainty in the reading of the reactions can be obviated by the use of a control. The test should be performed as follows. A sample of the toxin to be used should be heated to  $75^\circ$  C. for 5 minutes to destroy the soluble, specific toxic

fraction. On the right forearm the usual Schick test is made with a 1:1000 dilution of the unheated toxin, while a similar control injection is made on the left forearm, using an equal volume of a 1.5:1000 dilution of the heated toxin. The pseudoreaction shows a well marked redness after 48 hours at the site of both injections, but this fades rapidly so that by the end of 96 hours there is only a bluish brown area of pigmentation. Zingher (*Jour. Amer. Med. Assoc.*, Jan. 26, 1918).

Toxin-antitoxin immunization has reduced the diphtheria rate among nurses at the Durand Hospital from 13 to 0.53 per cent. The routine testing of prospective nurses and the immunization of those who were susceptible have practically removed diphtheria from the causes of sickness among nurses in a hospital devoted to treating contagious diseases. Crooks (*Jour. Amer. Med. Assoc.*, Jan. 17, 1925).

**Nasal Cases.**—The only cases that are difficult of diagnosis are those of primary nasal diphtheria. The thin, irritating, mucopurulent discharge, often brownish from the presence of blood, is quite different from the abundant, ropy mucus seen in simple catarrhal inflammation. Excoriation of the nares and eczema of the upper lip produced by the discharge are suggestive of diphtheria. Careful inspection may show the presence of more or less white or grayish-white exudate on the mucous membrane, in which case the diagnosis of diphtheria may be safely advanced. Furthermore, the diphtheritic cases are usually accompanied by some slight rise of temperature, anorexia, and a distinct degree of constitutional depression not seen in cases of simple inflammation. In diphtheritic rhinitis the lymphatic glands are usually enlarged, while in the simple forms of rhinitis glandular enlargement is infrequent. Finally,

these cases are much more often seen in institutions where the children are exposed to diphtheritic infection than in private or dispensary practice.

**Pharyngeal, or Tonsillar, Cases.**—

These often present difficulties in diagnosis, but a full consideration of all the factors in any case will usually lead to a correct judgment. The most difficult cases are the milder ones, where there is little or no membrane and the constitutional symptoms are slight. The question of exposure should be considered in every case. Children gathered in hospitals, or asylums, or attending schools are especially exposed to diphtheritic infection, and in them any form of sore throat may justly be looked upon with suspicion. So far as the catarrhal form of diphtheria is concerned, even with a history of exposure, there is no way of making a diagnosis of diphtheria in the early stages except by bacteriological cultures. The after-course of some of these cases—in which we may see invasion of the larynx, bronchopneumonia, nephritis, or paralysis—may show them to have been diphtheria when no suspicion has previously been entertained.

Case of a boy aged 7, supposed to have inspired a bead, accounting for existing cough and attacks of suffocation. Bronchoscopic inspection showed a little above and at the lower lobe bifurcation of the right lung, a membrane which bled on being loosened with a dull hook. Two hours later dyspnea became so urgent as to require immediate tracheotomy. Three days later the membrane was loosened under bronchoscopy and was removed piecemeal. Finally, the tube was removed on the seventh day. Nine months before, he had gone through a severe attack of diphtheria followed by cough. Skilern (*Laryngoscope*, Feb., 1917).

When diphtheritic membrane is present in the throat, it usually presents certain definite characters. It begins as a thin, translucent deposit upon one or both tonsils. Gradually or rapidly it becomes thicker, and assumes a white, gray or grayish-green, brown, or—in malignant cases—black color, and extends peripherally to cover a larger and larger area. It is firmly attached to the mucous membrane or underlying tissues and cannot be easily rubbed off. If removed by force, a raw, bleeding surface is left, and in a very short time the membrane is reproduced in its original or even a greater extent. Beginning upon the tonsils, the membrane rapidly extends to other parts: the lateral walls of the pharynx, the fauces, or uvula. Upon any of these parts the membrane presents the same characters as at the original site. This extension of the membrane is most characteristic of diphtheria. The only cases in which we are likely to see such extension of a pseudodiphtheritic membrane are the throat inflammations accompanying other infectious diseases, measles, small-pox, and—most of all—scarlet fever. The great majority of the membranous throat affections seen in the early stages of these diseases are produced by the action of streptococci or staphylococci. When a similar process is seen as a late complication of infectious disease, it is more probably true diphtheria.

The early temperature in diphtheria is not usually high; it is, in fact, generally lower than in pseudodiphtheria, with an equal amount of membrane. A high temperature in the beginning is, therefore, an indication that the case is not diphtheria. On the other hand, the prostration is greater in diphtheria than in pseudodiphtheria. The pulse is

feebler; the patients look and feel sicker than they do when suffering from pseudodiphtheria. The presence of a nasal discharge of a character described as belonging to nasal diphtheria and marked swelling and tenderness of the cervical lymph-nodes help to distinguish some cases in the early stages. Later we look for the development of the typical complications or sequelæ of diphtheria: invasion of the larynx, bronchopneumonia, albuminuria, or some of the manifold forms of paralysis. The occurrence of any of these processes is usually sufficient to make the diagnosis certain, although it is not impossible that any of them except the paralysis may be seen in cases of pseudodiphtheria. Paralysis subsequent to throat inflammation is seen only in diphtheria. Pseudodiphtheria is, in the great majority of cases, a milder disease and of shorter course than diphtheria. As already remarked, the primary throat inflammation of scarlet fever most closely resembles true diphtheria. In fact, in every case where diphtheria is suspected, the possibility of scarlet fever must be borne in mind and examination made for the eruption. Oftentimes it will be found at the very first examination; at any rate, a brief delay will suffice to determine the question, as the eruption of scarlet fever so quickly follows the initial symptoms. It may even happen that the throat symptoms of measles may simulate diphtheria, and especially if the eruption be delayed for a number of days. Here, however, there is rarely any membrane at all, and the presence of conjunctivitis, with the simple mucous discharges from nose and throat, should be sufficient to prevent mistake.

After tonsillotomy there is a fibrinous deposit on the stumps of the tonsils, but

the absence of constitutional disturbances, and, above all, the history, will prevent confusion with diphtheria.

The form of pharyngitis described by Vincent often gives rise to the appearance of a membrane which may resemble that seen in diphtheria. The deposit may be on one or both tonsils and may spread to the pillars of the fauces and to the posterior pharyngeal wall. This is not a true membrane, such as occurs in diphtheria, but is merely a necrosis of the surface epithelium. In Vincent's angina there is usually less prostration than in diphtheria, and the bacteriological findings in the former of the *Bacillus fusiformis* and *spirilla* and in the latter of the *Bacillus diphtheriae* will make certain the nature of the disease.

Furthermore, the presence of the spots described by Koplik is diagnostic of measles.

#### DIFFERENTIAL DIAGNOSIS.

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| 1. Exposure to infection from previous case of diphtheria.  | 1. No such exposure; arises independently.             |
| 2. Greatest liability in early years: first to fifth year.  | 2. Occurs at any age.                                  |
| 3. Membrane either seen from first upon pharynx, fauces, or uvula, as well as tonsils, or rapidly extends to these parts. | 3. Membrane limited to tonsils.                        |
| 4. Membrane firmly attached to underlying tissues, and not easily rubbed off.   | 4. Membrane loosely attached and easily removed.       |
| 5. If membrane be removed, leaves bleeding surface.   | 5. Membrane may be removed without such bleeding.      |
| 6. If removed, membrane is very rapidly reproduced in an even greater amount.   | 6. Reproduction of membrane not so rapid or extensive. |

#### DIFFERENTIAL DIAGNOSIS (CONTINUED).

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| 7. Discharge from nose thin, irritating, often bloody, and produces eczema of upper lip.           | 7. Nasal discharge not so common, and is simple mucopurulent.   |
| 8. Submaxillary and cervical lymph-nodes swollen and tender.                                       | 8. Swelling of lymph-nodes not so marked in primary cases; is regularly met with, however, in throat inflammations of scarlet fever, etc. |
| 9. Membrane may be seen upon buccal mucous membrane, tongue, angles of the mouth, or lips.         | 9. Not seen upon these parts.   |
| 10. Onset gradual; temperature low at beginning.   | 10. Onset more sudden; temperature higher.  |
| 11. Constitutional depression is more marked, the pulse weaker, and children more prostrated.      | 11. Constitutional symptoms usually in proportion to temperature; more moderate. Pulse rapid, but not weak, and depression not so marked. |
| 12. Course longer: usually five days to a week before marked improvement is seen.                  | 12. Course shorter, except in cases complicating infectious diseases; is usually three or four days.                                      |
| 13. Albuminuria common and severe nephritis frequent.  | 13. Much rarer.   |
| 14. Larynx often involved by extension.  | 14. Larynx rarely attacked secondarily, except in measles or scarlet fever.   |
| 15. Paralysis of more or less extensive groups of muscles may occur, as a complication or sequela. | 15. No such paralysis seen.   |

**Laryngeal Cases.**—When the laryngitis appears as the extension of a previous process in the nose or throat, except in the case of measles or scarlet fever, we can safely put it down as



diphtheritic. The pseudomembranous throat inflammations of measles and scarlet fever often involve the larynx, trachea, and bronchi, although the processes are not usually diphtheritic. In any other case such extension is almost conclusive evidence that we have to do with diphtheria. The greater difficulty is prevented by the primary cases of laryngitis in children. The characteristic feature of diphtheria of the larynx is its progressive, unremitting dyspnea with aphonia. The disease steadily advances to laryngeal stenosis and death from strangulation, unless relieved by treatment. Simple catarrhal, or non-diphtheritic, pseudomembranous laryngitis, on the other hand, usually shows frequent and decided remissions—its crises belonging to the night, the day showing decided remission of all the symptoms. As in the pharyngeal cases, early high temperature belongs rather to the pseudodiphtheria. If laryngeal examination be possible and we can see and determine the character and extent of the membrane in the larynx, we ought to be able to reach a positive diagnosis; but, unfortunately, such examination is not practicable among young children, who furnish the great majority of the cases of acute laryngitis. Of 283 cases of acute laryngitis subjected to bacteriological examination by the New York Board of Health, 229—or 80 per cent.—proved to be true diphtheria; so that in the city, at least, the diagnosis in any such case would incline to diphtheria.

While it is true that, as many authorities maintain, in 95 per cent. of the cases which an expert, after careful consideration, would pronounce diphtheria, cultures will show the presence of the specific bacillus, it must be frankly admitted that there are many

cases in which the most careful observation cannot determine positively the question whether a given case is true diphtheria or pseudodiphtheria. Thus, in Scientific Bulletin No. 1, of the New York Board of Health, we find it stated that "Baginsky, in Berlin, found the diphtheria bacillus in 120 out of 154 suspected cases; Martin, in Paris, in 126 out of 200; Park, in New York, in 127 out of 244; Janson, in Switzerland, 63 out of 100, and Morse, of Boston, in 239 out of 400. Thus, from 20 to 50 per cent. of the cases sent to diphtheria hospitals did not have diphtheria." If these figures approximate the truth, it is evident that we cannot trust with safety to clinical observations to determine the specific relation of cases of throat inflammation. On the other hand, the routine use of cultures from all cases of sore throat regularly shows the presence of the diphtheria bacillus in a considerable number of cases in which there were few or none of the features regarded as characteristic of diphtheria, and in which there was; therefore, little or no suspicions of the presence of the specific bacillus.

While so far as the individual case is concerned, it may be remarked that the cases in which the diagnosis is most difficult are the mild cases, those least likely to be attended with grave consequences to the patient himself, the fact should also be recognized that these mild cases are quite as dangerous to others as severe ones, and should, for the sake of the community, be subjected to strict quarantine. It is, therefore, essential to accurate work and proper care, as well as proper prophylaxis, that cultures should be made from all cases of sore throat. In no other way can we stand upon solid ground with relation to treatment, or hope to eventually gain

control of the widespread and dangerous infection.

In 529 cases, the laboratory workers' diagnosis agreed with the clinical diagnosis made by the hospital medical officer in 97.5 per cent. Caiger and O'Brien (*Lancet*, July 12, 1924).

**Methods of Making Bacteriological Examinations.**—An immediate microscopic examination of the exudate in cases of suspected diphtheria will often justify a positive diagnosis. A bit of membrane removed from the throat by a swab is smeared upon a cover-glass or slide, dried, fixed by heat, and then stained with Löffler's methylene-blue solution.

With an oil-immersion lens we may then be able to determine the presence of bacilli sufficiently characteristic to warrant a positive diagnosis. The bacilli under such conditions do not have the characteristic features which are presented by cultures upon suitable media. They are much more irregular in size, shape, and staining properties. Positive judgment is, therefore, much more difficult and uncertain. Failure to find the bacilli by this method would in no way prove that the case was not diphtheria. The uncertainties of the method are so pronounced that it is rarely employed.

The best culture medium for routine work is the Löffler blood-serum, coagulated by heat in test-tubes in such a way as to give an extensive slanting surface for inoculation. It is important that the reaction of the medium be neutral or slightly alkaline, for the diphtheria bacillus grows very poorly on acid media. The swabs used in obtaining the infected material from the throat are made by wrapping a small quantity of absorbent cotton about the end of a small steel rod six inches in

length. The swabs so made are inserted into test-tubes, which are then plugged with cotton and the whole sterilized by exposure to dry heat at 150° C. for one hour. To make a satisfactory culture a good view of the throat must be obtained and the swab rubbed upon the surface covered by the edge of the membrane, or—in the absence of membrane—upon the inflamed parts. In laryngeal cases where no membrane is visible it usually suffices to make the application of the swab either to the tonsils or as low in the pharynx as possible. In such cases if the first culture fails to show the presence of diphtheria bacilli, it is always well to repeat the process, as second or third culture may show the bacilli previously absent from the accessible parts of the throat. Care must be taken in inoculating the swab not to allow it to touch the tongue or any other part or surface than the one upon which the presence of the bacilli is suspected. Otherwise contaminating bacteria are inoculated upon the culture media and the value of the culture for diagnostic purposes destroyed.

To carry out these directions in young children it is necessary that they be carefully held. The best method is to have the mother or nurse hold the child upon her right side, the child's face turned toward the light and the head resting upon her right shoulder, one of the holder's arms about the patient's legs, the other controlling the arms. The physician can then usually insert a tongue depressor and control the head with one hand, while with the other the swab can be properly directed. With very fractious children it may even be necessary to have a second assistant hold the child's head. Failure to take pains in making a proper application of the swab is accountable for many of the

unsatisfactory results obtained from cultures. The swab having been properly inoculated, the cotton stopper is withdrawn from the mouth of the tube containing the solidified blood-serum and the swab then rubbed gently over the surface of the culture medium, care being taken not to break the smooth surface of the medium. The swab is then withdrawn, the cotton stopper, which must have been held so as to have escaped contamination from any outside source, replaced in the mouth of the culture-tube, the swab dropped into its tube again and confined by its own stopper. The culture-tubes are then ready for incubation. Koplik has described a rapid method of incubation and examination in which he allows only two or three hours' incubation at 37° C., at the end of which time he asserts that the growth of the diphtheria bacilli is more characteristic than at any other period of incubation.

When there is no special reason for haste, it is usually more convenient to adopt the method followed by the New York Board of Health, of twelve hours' exposure; the cultures are kept at body temperature overnight, and are ready for examination in the morning.

It is not possible to determine the presence or absence of diphtheria bacilli in the cultures upon the blood-serum from the gross appearances; but if it is found that the culture medium has been liquefied during the incubation, it can safely be said that contaminating bacteria are present in such numbers as to render the culture valueless. The diphtheria bacilli or cocci do not liquefy the medium.

Upon the center of a clean cover-glass is placed a drop of sterile water. With a sterile platinum loop a number of the colonies, which show themselves

as fine, granular elevations upon the culture surface, are swept off. The loop is then immersed in the water upon the cover-glass and its contents spread evenly over the glass. The preparation after being allowed to dry in the air is fixed by passing it three times through a moderate gas flame. It is then stained by covering it with Löffler's alkaline methylene-blue solution and allowing it to stand for ten minutes, or Neisser's diphtheria stain can be used. The cover-glass is then washed, dried, and mounted in Canada balsam.

The examination is made with a  $\frac{1}{12}$  oil-immersion lens. In a large proportion of the cases we see an almost pure culture of the diphtheria bacillus; next most frequently cultures of cocci, single, double, or in chains; in some cases the cocci and bacilli are about equal in number, and in a small number only a few diphtheria bacilli are seen scattered among great numbers of cocci. From time to time we see in the cultures bacilli which closely resemble the diphtheria bacilli, but with certain definite points of distinction, and pseudodiphtheria bacilli. The diphtheria bacilli seen in such cover-glass preparations vary in length from 1.5 to 6.5 micra, and in diameter from 0.3 to 0.8. They occur singly or in pairs, rarely in chains of three or four. The rods are straight or slightly curved and are not usually uniformly cylindrical throughout their length, but are swelled at the ends, or pointed at the ends and swelled in the middle. The variety in size and shape, even from the same culture, is characteristic. When in pairs, the bacilli may lie with their axes in the same line or forming an acute or obtuse angle; sometimes they are crossed. The bacilli show no spores, but may contain highly refractile bodies, especially in their

swelled portions. When grown upon blood-serum and stained in the manner above described, the bacilli stain in a peculiarly characteristic way. Lack of uniformity, both in the individual bacillus and in the numbers of groups, is marked. Thus, different parts of a bacillus take the stain unequally; so that the ends are dark blue, while the center shows little or no color, or *vice versa*. Likewise bacilli lying side by side show marked difference in coloring, one being much more deeply stained than the other. This lack of uniformity in the staining of the bacilli seems to belong to a certain period of their growth; it is usually marked after the twelve-hour incubation, but may disappear entirely in older cultures.

Mention has already been made of bacilli found in cultures resembling the diphtheria bacillus and yet not possessing the specific pathogenic properties of that bacillus, and therefore termed pseudodiphtheria bacilli. This term is most unfortunate, since these bacilli bear no relation to the throat inflammation termed pseudodiphtheria. As seen in cover-glass preparations, these bacilli are shorter, plumper, and more uniform in size and staining. They are most often met with in cultures from the nose. When obtained in pure cultures, these bacilli have been shown to be devoid of virulence.

As seen under the microscope, the uniformity in size, shape, and staining is sufficiently marked from the variations in these points noted with reference to the diphtheria bacillus to enable practised observers to recognize them readily.

Whenever we find the characteristic bacilli above described present in the cover-glass preparations, we can safely set the case down as one of true diph-

theria, however few the bacilli may be in number in the smear, or with whatever other bacteria combined. If the diphtheria bacilli are found at all, a second culture usually shows them greatly exceeding in numbers any other form of bacteria present, and the cases will be found to present the clinical symptoms of diphtheria.

In any case, to render the bacteriological diagnosis complete, it would be necessary to obtain the diphtheria bacilli in pure culture and test their virulence by inoculation of susceptible animals.

In routine practice this is done by inoculating half-grown guinea-pigs with from  $\frac{1}{4}$  to  $\frac{1}{2}$  per cent. of their body weight of a forty-eight hours' culture of the bacilli grown at 37° C. in simple nutrient or glucose alkaline broth. In carrying out such experimentation many precautions are necessary to render such work accurate and trustworthy. Much time and labor are consumed in the process. For our purposes it is sufficient to know that the great majority of those who have carried on such experiments under proper conditions with bacilli derived from pseudomembranes and presenting the morphological and staining characters of diphtheria bacilli have found the bacilli fully virulent.

So long as the bacteriological diagnosis is reinforced by clinical evidence of the presence of false membrane and the symptoms of diphtheria, we can safely trust to the examination of these cover-glass preparations.

We find, however, that the examination of healthy throats has led to some remarkable results. In the throats of those who have been exposed to diphtheria, but have remained perfectly well, we may find characteristic and fully virulent diphtheria bacilli; in others we may find the pseudodiphtheria bacillus

already spoken of, or a bacillus which, while presenting the cultural and morphological characters of the diphtheria bacillus, proved in inoculations to be non-virulent.

Thus, in a series of 330 healthy throats examined by the New York Board of Health, in 8 virulent characteristic diphtheria bacilli were found, in 24 non-virulent characteristic diphtheria bacilli, and in 27 non-virulent pseudodiphtheria bacilli. Since Hofmann's observation of these bacilli, so closely resembling the Löffler bacillus, but devoid of virulence, a great deal of attention has been given to this subject. Opinion is still divided as to the relation of these non-virulent bacilli. On the one hand, they are regarded simply as degenerate or attenuated forms of the diphtheria bacillus; on the other, they are represented as a distinct species.

The identity of the pseudodiphtheria bacillus seems to be now established. In form these are smaller, shorter, and thicker than the diphtheria bacillus. When seen in stained smears the bacilli are often observed to be lying parallel to one another, in contrast to the irregularly angular disposition of the diphtheria bacillus. In their growth in broth the pseudodiphtheria bacilli develop alkali, whereas the Löffler bacillus forms acid. They are never virulent. These differences are, by most authorities, considered sufficient to warrant the belief that they are a separate species.

The other class of non-virulent bacilli found in the throat present all the characters of the Löffler bacillus except their virulence. Roux and Yersin believed these bacilli to be simply attenuated forms of the diphtheria bacillus. It was shown that they are particularly likely to be met with in the throats of those who have had diphtheria some

time before, or have been exposed to diphtheria. It was also found that the diphtheria bacillus could be so attenuated by various methods of growth as to deprive it of its virulence. No one, however, has yet been able to restore virulence to any of the non-virulent forms met with, and the question must be considered as still open.

Dependence upon clinical symptoms in a case of sore throat, whether with restricted or more marked exudation, is apt to be misleading. Differentiation depends wholly upon the presence or absence of the Klebs-Löffler bacillus. In all suspicious cases, a throat swab should be submitted at once to a laboratory and the case isolated until the report is received. Particularly in small children, and also in older individuals up to the age of 20 or 25 years, no delay in specific treatment should be permitted, but antitoxin should be given at once even in an only slightly suspicious case, without waiting for laboratory confirmation.

In early suspected laryngeal cases, considerable diagnostic help may be obtained from *laryngoscopy*. As E. T. Gatewood (Va. Med. Mthly., Jan., 1922) states, it rarely becomes necessary to intubate in laryngeal diphtheria if the condition is diagnosed early. A satisfactory culture can be obtained from infants and children in such cases only by direct laryngoscopy. The distally illuminated laryngoscope, patterned after Jackson, is preferred for this purpose, and if it is inserted gently along the median line until the epiglottis is caught behind the spatula, no harm can possibly be done. A membrane seen on the larynx demands prompt use of antitoxin without a positive culture. Otherwise, cultures from the larynx are essential to diagnosis in the early stage.

The authors advocate the method of Bordet and Gengou, of fixation of the complement, for a rapid, early, sure diagnosis. As antigen they employed an emulsion in salt solution of the mucus obtained from the tonsils and pharynx on a cotton tampon. Antidiphtheritic serum from the Pasteur Institute contained the amboceptor, and fresh rabbit serum the complement. A sheep hemo-

lytic system was employed. Twenty-five cases of diphtheria resulted in fixation; 10 cases of non-diphtheritic angina, 9 of measles, and 3 of scarlatina showed hemolysis and were negative. Weil-Hallé and Block-Michel (Bull. et mém. de la Soc. méd. hôp. de Paris, vol. xxvii, p. 707, 1910).

Toluidin blue gives a better differentiation than any yet devised, and the technique is simple. The writer uses toluidin blue, 0.02 Gm.; glacial acetic acid, 1 c.c.; absolute alcohol, 2 c.c., and distilled water, to make 100 c.c. A smear is taken fresh from the throat, and, when fixed on a cover-glass, is stained by placing a thin drop of the stain directly upon it and inverting it to make a hanging-drop preparation. This is then examined by artificial light, the blue of the fluid tending to neutralize the yellow rays. The diphtheria bacilli stain a light blue with red granules, and are refractive. They are differentiated from pseudodiphtheria bacilli at once. Ponder (Lancet, July 6, 1912).

When circumstances demand exact differentiation, cultures on coagulated serum of the true diphtheria bacilli are dry and white, while those of the Hofmann bacillus are moist and yellow. The diphtheria bacilli are slender, with numerous granulations, the rest of the protoplasm of an even, pale tint, not taking or retaining stains well. Hofman (Bull. de la Soc. méd. des hôp. de Paris, July 27, 1917).

The writer has used for 8 years the following mixture: Toluidin blue, 0.1 Gm.; glacial acetic acid, 0.5 c.c.; distilled water, 100 c.c. A drop of stain is put on each film and a cover-glass is then placed over the preparation. The excess of stain is removed by blotting each slide between 2 layers of blotting paper immediately before being examined. The first slide is ready for examination about 1 minute after the stain is applied, and the others are taken in rotation. The best results are obtained by using strong artificial light. When slides are stained in this way the polar

granules of *B. diphtheria* are of a deep reddish purple, while the bodies of the bacilli appear faintly blue. Most of the organisms found in diphtheria swabs, including Hofmann's bacillus, are more faintly stained, so that *B. diphtheria* is readily detected when present only in small numbers. The stain may also be used in a similar manner for demonstrating the bacillus in smears made directly from the swabs, in which case the film should be allowed to stand in the stain for from 2 to 3 minutes. Sutherland (Lancet, Feb. 8, 1919).

In primary *tracheobronchial diphtheria*, the usual cultures are negative. The most suspicious sign is the gradual onset of persistent and progressive dyspnea. At first the breathing is wheezy; then inspiratory stridor manifests itself, with croupy cough, while the voice remains clear. Air-hunger supervenes, with restlessness. In 1 such case in a trained nurse an early clinical diagnosis was made; laryngoscopy showed membrane protruding from the trachea and recovery occurred under 40,000 units of antitoxin. A similar result was obtained in a child of 18 months. H. Dupuy (New Orl. Med. and Surg. Jour., Sept., 1923).

A *staphylococcic pseudodiphtheria* was found by the writer in 10 cases. Laryngeal obstruction was always preceded by tonsillitis, sometimes with pseudomembranes. Antitoxin, even when given early, proved useless, and in 4 cases **tracheotomy** became necessary. The cases responded rapidly to **staphylococcus vaccine**, however, and no deaths occurred. Infected skin lesions, especially impetigo, in the patient or his associates, should suggest a staphylococcic infection. In doubtful cases of croup not responding to antitoxin, both the latter and staphylococcus vaccine should be given until bacteriologic evidence is obtained. The vaccine also proved beneficial in 4 cases of laryngismus stridulus. Brisset (Bull. Soc. nat. de chir., Mar. 29, 1924).

Smears from a large number of swabs showed the diphtheria bacillus in about 60 per cent. of the positive cul-

tures. The organisms of Vincent were found in many cases which were clinically confused with diphtheria. Smears from both the swabs and cultures were stained with Löffler's alkaline methylene blue and a diagnosis made on staining reaction, morphology and arrangement. Young and Crooks (Jour. Lab. and Clin. Med., Sept., 1925).

**ETIOLOGY.**—As early as 1879 Klebs is said to have observed the presence of a peculiar bacillus in cases of diphtheria. In 1883 his observations of the presence of this bacillus in the pseudomembranes from the throats of those dying of epidemic diphtheria were reported and brought to general attention. In 1884 Löffler published the results of his observations. He had found the bacillus present in the great majority of cases diagnosed as diphtheria, had been able to obtain the bacillus in pure culture, had inoculated it upon the abraded mucous membranes of susceptible animals and thereby produced pseudomembranous inflammation, often followed by death; he had injected bouillon cultures of the bacillus subcutaneously and had found characteristic lesions after the death of the animals so treated. In 1888 d'Espine found the bacilli present in 14 cases of typical diphtheria, and proved them to be absent in 24 cases of mild sore throat not presenting the clinical characters of diphtheria. In the same year Roux and Yersin reported that they had found bacilli presenting the characters described by Löffler in all cases of typical diphtheria. They showed that when inoculated upon the healthy mucous membrane of the trachea of rabbits no effect was produced; but, if the membrane were previously abraded, the symptoms of pseudomembranous laryngitis in man followed: congestion of the mucous membrane, the formation of pseudo-

membrane, swelling of the glands and cellular tissues of the neck, dyspnea, stridor, and asphyxia. From that time on numerous observations were made in France, Germany, and America, until, in 1891, Welch declared that all the conditions necessary to the demonstration of the specific relation of the Klebs-Löffler bacillus to diphtheria had been met: (1) its constant presence in cases of true diphtheria; (2) its isolation in pure culture, and (3) the production of all the symptoms of the disease by the inoculation of pure cultures in susceptible animals. Since that time evidence has been accumulated from many sources, till there can no longer be any doubt that the essential cause of diphtheria is the growth and development of this bacillus within the body. The disease must, therefore, be dependent in every case upon the presence and action of the diphtheria bacillus.

The disease is common in all parts of the land. In the cities it is usually endemic, the frequency and virulence of the disease varying from year to year; in rural communities it usually occurs as distinct epidemics, each new outbreak being dependent upon the introduction of the disease from without. It may also occur sporadically. It does not, however, in any case arise *de novo*. Each new case is developed by infection, however remote, from some previous one. The infection may be direct or indirect, most commonly the former.

The bacilli are usually present in great numbers in the discharges from the throat or nose of the patients, in the saliva, and in the membranes which may, from time to time, be coughed up. They are not, so far as evidence is had, present in the breath of the patients, but may abound in the air of the room or rooms inhabited by them. The bacilli

have even been reported as present in the urine of patients.

Direct contact with the discharges from the nose or throat of those suffering from diphtheria is most dangerous. Many a physician has fallen victim to diphtheritic infection received by allowing a child to cough in his face during the process of examination. Kissing the patients may likewise be the means of infection in many cases.

While severe cases are usually due to the action of virulent bacilli and may, therefore, be especially potent in transmitting the disease, it is not to be forgotten that apparently mild cases may harbor bacilli just as virulent and just as much to be avoided. As already remarked, the most virulent bacillus Park has met with was derived from a mild case of diphtheria. The cases of virulent pharyngeal diphtheria are most dangerous on account of the quantity of the discharge. Purely laryngeal cases have little or no discharge, and are consequently less likely to spread the infection.

The bacteria may linger in the throat for weeks after the disappearance of all clinical symptoms and the patients continue throughout the period to be sources of infection.

Indirect infection may occur by means of the clothing of the patients, the bedding, carpets, wallpaper, draperies, eating or drinking utensils, tongue-depressors, swabs, instruments of any kind used upon or about the patient, anything that has come in contact with the infectious discharges. Children's toys or books are especially likely to be contaminated and become means of carrying the germs to others.

The urine has been found to contain diphtheria bacilli long after the patient had recovered, several months

in some instances. They have also been found in feces.

The writer, with Haas, has published an article on anal diphtheria, and the presence of bacteria in the feces. This makes it imperative to disinfect these excreta as well as the urine. Delbanco (*Deut. med. Woch.*, Nov. 12, 1912).

Virulent diphtheria bacilli reach the urine in about one-third of all cases and are often in position to propagate the infection. The danger of direct contact infection is slight because of the great dilution, there being relatively few bacteria present in a given bulk of urine. Yet under favorable conditions the urine might contaminate the milk vessels and so infect a milk supply. In theory the urine might infect the patient's skin, causing, for example, diphtheritic vulvitis. Conradi and Bierast (*Deut. med. Woch.*, Aug. 22, 1912).

Diphtheria bacilli found in the urine in all of 19 children examined when they had supposedly entirely recovered from diphtheria. The interval at date of writing was from four to eight weeks up to fourteen weeks, and in 6 of the 8 cases in which animals were inoculated with the bacilli they proved virulent. Strict hygiene would require the isolation of the children until the urine was free of bacteria. Beyer (*Münch. med. Woch.*, Feb. 4, 1913).

Apart from the question of the transmission of the disease from case to case, many other factors may influence the development and spread of diphtheria.

Sex apparently has no influence, but age materially influences the susceptibility. Nursing children are usually immune and contract the disease only by continued close contact with those suffering from it. The greatest susceptibility lies between the ages of 2 and 5 years; from 5 to 10 many cases are seen; after 10 the susceptibility diminishes very rapidly, and in adults it is but slight. The following table of 14,688 deaths occurring in New York in ten



years, tabulated by Billington, illustrates these points:—

Under 1 year .....	1,214
From 1 to 5 years .....	9,622
From 5 to 10 years .....	3,212
From 10 to 15 years .....	311
Over 15 years .....	329

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Total ..... 14,688

In 1000 deaths due to diphtheria, 20 per cent. occurred in children less than 1 year of age; 25 per cent. between 1 and 3 years; 62 per cent. of all deaths occurred before the age of 5. Laryngeal diphtheria was far more prevalent than other forms; pharyngeal was next, and the nasal form last. A culture should be taken in all conditions where there is a possibility, even though remote, of diphtheria. B. W. Carey (Boston Med. and Surg. Jour., Jan. 16, 1919).

The season of the year exerts some influence. Thus, in England and Wales the average number of deaths for each quarter of the year, from 1870 to 1893 inclusive, was as follows: First quarter, 1000. Second quarter, 819. Third quarter, 847. Fourth quarter, 1192. (Thorne.)

Diphtheria is, therefore, more common during the cold months of fall and winter than during the spring and summer. The same fact is borne out by Bosworth's analysis of 18,688 deaths from diphtheria occurring in New York during thirteen years. Of these, 10,769 occurred from October to March, and 7919 from April to September, inclusive.

The massing of children in schools, asylums, and hospitals produces conditions favorable to the development and spread of diphtheria, doubtless by increasing the chances of infection. The schools have often been pointed out as the sources of epidemics of diphtheria, which could only be controlled by closing the institutions concerned.

The following section from the Bulletin of the New York Board of Health is of interest in this connection:—

"It has been the practice of the Department to plot upon a city map the location and date of every case of diphtheria in which the diagnosis had been settled by bacteriological examination. After several months the map presented a very striking appearance. Wherever the densely settled tenements were located, there the marks were very numerous, while in the districts occupied by private residences very few cases were indicated as having occurred. It was also apparent that the cases were far less abundant, as a rule, where the tenements were in small groups than in the regions of the city where they covered larger areas. At the end of six months there were square miles in which nearly every block occupied by tenement houses contained marks indicating the occurrence of one or more cases of diphtheria, and in some blocks many (15 to 25) had occurred.

"As the plotting went on, from time to time the map showed the infection of a new area of the city, and often the subsequent appearance of an epidemic. It was interesting to note two varieties of these local epidemics: in one the subsequent cases evidently were from neighborhood infection, while in the second variety the infection was as evidently derived from schools, since a whole school district would suddenly become the seat of scattered cases. At times, in a certain area of the city from which several schools drew their scholars, all the cases of diphtheria would occur (as investigation showed) in families whose children attended one school, the children of the other schools being for a time exempt."

A number of epidemics have been

traced to infected milk, the infection arising from the presence of diphtheria among those engaged in handling the milk.

Certain English observers have also claimed to have discovered a specific disease among milch cows, characterized by an eruption of vesicles and pustules upon the udders and teats, accompanied by the presence of the diphtheria bacillus in the local lesions, and capable of being reproduced by infections of the bacilli.

Other outbreaks of diphtheria have been attributed to bad drainage, defective sewers, or the presence of an abundance of decomposing organic matter. It is also held that certain domestic animals—pigeons, cats, etc.—are susceptible to diphtheria and may be the means of transmitting it to man.

During the World War, some wounds were stated to have contained diphtheria bacilli. In most instances, however, these proved to be diphtheroids.

In September, 1917, a report was published by Fitzgerald and Robertson upon the presence of the diphtheria bacillus in wounds of returned soldiers. They found no less than 40 out of 67 cases yielded cultures of *B. diphtheria*. These findings led to a study of 306 cases. Of these 56 showed the presence of diphtheroid organisms, while 2 contained bacteria yielding all the characteristics of the *B. diphtheria*. Adami, Bowman and others. (Can. Med. Assoc. Jour., viii, 769, 1918).

Skin diphtheria would be found oftener if cultures were taken from slow healing wounds. In each of 2 cases a finger was the seat of the infection. In 1 of the cases the knee and dorsum of the foot were also affected. In this case, treatment consisted in removing the necrotic tissue with a sterile applicator and applying 10 per cent. silver nitrate once a day. Friedel (Minn. Med., Nov., 1925).

The writer confirmed Feiler's experiments to the effect that *trypanflavin* in a dilution of 1:100 or even 1:1000 is capable of neutralizing experimental diphtheritic infection of skin wounds in guinea-pigs. Reinhardt (Zeitschr. f. Hyg. u. Infekt., Jan. 17, 1922).

However much or little insanitary surroundings may contribute to the development of diphtheria, the active and essential cause must be the diphtheria bacillus, and our plans for limiting the ravages of this disease must include the control of the individual cases, each of which is a focus for the farther spread of the infection.

The tenacity to life of the bacillus outside the body is remarkable. Hofmann found that it would live for 155 days on blood-serum; Löffler and Park for 7 months, and on gelatin Klein found it living after 18 months. On bits of dried membrane Klein found living bacilli after 14 weeks, Park after 17, and Roux and Yersin after 20 weeks. Abel says that, dried on silk threads, they may live 122 days, and upon a child's plaything kept in a dark place he found the bacilli alive after 5 months.

The period of incubation of diphtheria varies from two days to a week. It is doubtless affected by the number and virulence of the organisms present and by the resisting power of the patient. In most cases it is impossible to determine the time of exposure, much less that of infection. Second attacks of diphtheria are rare, but do occur. In one case observed at the New York Foundling Hospital, a boy of 4 had croup in March. The diphtheria bacilli were demonstrated in cultures from the throat. Antitoxin was given and he recovered. Twenty-five days later, having been apparently well in the mean time, he developed tonsillar diphtheria, which

extended to the larynx; pneumonia developed, and death followed, thirty-four days from the conclusion of the first attack. According to Zucker, second or third attacks comprise 9 to 13 per cent. of all cases of diphtheria.

**Transmission by Carriers.**—In some cases persons who are themselves perfectly healthy, but who have been in contact with diphtheria cases, are found to harbor the bacilli in the nose or throat and may be the source of infection to others. On several occasions the development of a series of cases of diphtheria in a single nursery of the New York Foundling Hospital has led to the examination by cultures of the throats of all children in that nursery, with the result of usually finding two or three who, while apparently healthy, had typical germs in their throats.

Considerable light was thrown on the carrier state by the investigations of Moss, Guthrie and Marshall (Bull. Johns Hopkins Hosp., Feb., 1921). They found that inoculation of human beings with avirulent diphtheria bacilli could be readily effected without causing any symptoms or change in the appearance of the throat. The resulting carrier state was persistent, 2 carriers still harboring the bacilli 15 months later. Antitoxin did not prevent the lodgment and growth of the organisms. No cases of clinical diphtheria developed among the associates of these "healthy carriers." After prolonged sojourn in the throat the bacilli showed no change in morphology or other characteristics and no tendency to become virulent. Spraying the nose and throat with a tolerable gentian violet solution seemed without effect in eradicating the avirulent bacilli. Inoculating bacilli virulent for guinea-pigs in 8 volunteers, Guthrie, Marshall and Moss (Bull. Johns Hopkins Hosp., Dec., 1921) observed the 4 with positive Schick test fall ill with diphtheria and all become carriers after their recovery. Of the 4 with negative Schick tests, none developed the disease, but 3 became carriers.

Out of 91 infants with purulent otitis media in an institution, Davidsohn and Heck (Berlin. klin. Woch., Aug. 29, 1921) found diphtheria bacilli in 28. Some were virulent and others avirulent. There were no evidences of toxemia and the germs are believed to have been secondary invaders. In the infants with the most persistent ear discharges the bacilli were nearly always found. The possibility of diphtheria transmission in this way should receive due consideration. The organisms were made gradually to disappear by syringing of the ear with **formalin** solutions.

This question of diphtheria bacilli carriers has received considerable attention. In a study by the writers a total of 784 smears were taken, including some from the relatives of 44 of the children. The number of carriers invariably showed a marked increase when a child entered who had recently passed through diphtheria, or a child developed it in the school or ward. The closer neighbors of the diphtheria case nearly always had diphtheria bacilli in their throats. Renault and Lévy (Arch. de méd. des enfants, Sept., 1915).

Long clinical experience showed the curative value of a **coating of oil** applied to the nasopharyngeal mucous membrane in diphtheria, influenza, pertussis, tonsillitis, etc. For this purpose **jasmine oil** was most satisfactory, being non-irritating. With the patient reclining and head thrown far back, half a medicine dropper full of the oil should be introduced into the nostrils drop by drop. The position should be retained for a minute, after which the head should be rotated, first to one, then to the other side. William Ewart (Brit. Med. Jour., Dec. 11, 1915).

To verify the report of Friedberg, Ruh, Miller, and Perkins that certain persistent diphtheria carriers gave negative cultures after tonsillectomy and removal of adenoids, the writer studied the tonsils from 7 diphtheria carriers all of whom had had positive cultures from nose or throat for 21 days or over. Tonsils from 14 pa-

tients who had undergone tonsillectomy for various other causes were used as controls. In the tonsils of the 7 diphtheria carriers, 6 showed Gram-positive beaded bacilli in large numbers. These were found chiefly in the crypts, in the plugs of tissue and in the tissues lining the crypts in which the epithelium was very thin. Of the 14 pairs of control tonsils studied only 2 showed any Gram-positive bacilli. Cleaning up of diphtheria carrier cases by tonsillectomy is due to the removal of an important focus of infection. Brown (*Jour. Infect. Dis.*, Oct., 1916).

Several instances are recorded by the writer in which, after **tonsillectomy** and **removal of adenoids**, disappearance of the bacilli occurred in 2 days. S. A. Friedberg (*Jour. Amer. Med. Assoc.*, Mar. 11, 1916).

The writers freed 88 carriers of bacilli by an average of 19.1 applications of 1 per cent. **mercuochrome** solution with the medicine dropper, spray, or swab. Two more resistant cases continued to harbor the bacilli in the tonsillar crypts and scars of a peritonsillar abscess, though a 2 per cent. solution was used. Gray and Meyer (*Jour. of Inf. Dis.*, Apr., 1921).

A jet of **superheated air** directed on the throat for 10 or 15 minutes seemed effective, the 50 patients becoming bacteria-free usually after 3 to 5 applications. De la Rivière (*Bull. de l'Acad. de méd.*, May 3, 1921).

The writer uses the same procedure as Rivière for 5 or 10 minutes twice a day, plus **insufflation of powdered antitoxin** into the nasal cavities and nasopharynx at night. Audouard (*Bull. Soc. méd. des hôp. de Paris*, Feb. 4, 1922).

The writers used 5 per cent. **mercuochrome** and saturated **gentian violet** solutions in separate groups of scarlet fever cases with diphtheria infection. The solutions were swabbed in the nose and throat twice daily for 3 days, 24 hours elapsing before the culturing. The first agent cured 68 per cent., the second 62 per cent., while of the controls, 34 per cent. cleared up without the treatment. Estabrook and Lincoln

(*Jour. Mich. State Med. Soc.*, Jan., 1922).

Negative throat cultures were soon obtained in several carriers treated as follows: On awakening, after each meal, and during the evening, the nares and fauces are flushed with saline solution to remove mucus. They are then at once sprayed with 2 per cent. **gentian violet** solution. A culture is taken just before 1 of the treatments. When 2 negatives have been obtained, the dye is discontinued and another culture taken 48 hours later. The patient and family should be warned that the dye will stain everything but the skin, mucosa and teeth. J. S. Saurman (*Jour. Amer. Med. Assoc.*, July 26, 1924).

The writer recommends **ether inhalations** by the open method every morning for 5 days, sufficient anesthetic being used to produce marked drowsiness. R. I. Longabaugh (*U. S. Naval Med. Bull.*, Aug., 1924).

Data showing that 152 out of 185 carriers treated with the **X-ray** tended to remain free of virulent organisms after an interval of 90 days. In another series of 23 cases, negative cultures were obtained after 1 or at most 2 treatments. A broad focus Coolidge tube, 10 in. focal skin distance, 7 in. gap, 5 ma., and 3 mm. aluminum filter were used. Both the tonsillar areas and postnasal space were treated at each sitting. D. Kahn (*Amer. Jour. of Roentg.*, Oct., 1924).

The writer uses a 10 per cent. **ichthyol** ointment, applying as much of it as the end of a swab will hold. Using one swab for each cavity, the ointment is applied to the nasal surfaces and nasopharynx 5 days in succession. Israeli (*Jour. of Lab. and Clin. Med.*, Apr., 1925).

The isolation of these children would at once break the succession of cases of diphtheria previously observed. It may also happen that physicians or nurses transmit the germs either by their hands or clothing from one case to another. The

frequent occurrence of diphtheria in the families of physicians is sufficient evidence of the need of care.

**PATHOLOGY.**—The bacteriological investigations of recent years have materially affected our views of the pathology of diphtheria. We have learned that the local lesions of the mucous membranes really constitute a very subsidiary part of the process. In them the diphtheria bacilli grow and multiply, developing in their growth certain organic substances, termed toxins, which are readily absorbed into the circulation and by their action produce constitutional symptoms and remote affects more characteristic of the disease than the local lesions themselves. The diphtheria bacilli have been found not only upon the mucous membranes, but in the lungs, liver, spleen, lymph-nodes, kidneys, and even upon the valves of the heart. They are not, however, present in great numbers in any of these organs; in fact, they are, except possibly in the case of the lungs, so few in number as to be demonstrable only by means of cultures. Their presence in the viscera does not excite characteristic lesions of these parts, and seems to be an accidental accompaniment rather than an essential part of the disease.

The diphtheria bacillus present in the blood and cerebrospinal fluid. In the blood it is said to occur in less than 5 per cent. of cases. The bacillus likewise enters the cerebrospinal fluid in at least one-half of all cases. In a study of the lungs at the Hamburg-Eppendorf Hospital, in 67 cadavers (of which number 43 had died during the period of disease and the rest after the disease proper had run its course) diphtheria bacilli were found in the lungs in 56 subjects (85 per cent.). In all but 6 cases of the positive finds other bacteria were present, chiefly erysipelatus streptococci. In the negative cases the microbic finds were insignificant. The

association of the Klebs-Löffler and Fehleisen bacteria in so many cases (27 in all) was at least suggestive. Reye (Münch. med. Woch., Oct. 29, 1912).

The action of the toxins is characteristic and important. These substances have been isolated and studied especially by Brieger and Fraenkel, Roux and Yersin. They have been found to be allied to the albumins, and have been designated as toxalbumins. In experimental inoculations in susceptible animals, as shown by Welch and Flexner and others, they have been found to produce all the characteristic features of diphtheria except the membrane, especially the characteristic post-diphtheritic paralysis. The most striking of their remote effects are produced in the lymph-nodes and liver. In the lymph-nodes they produce a distinct hyperplasia; in the liver necrosis or death of small areas of liver-cells, focal necroses, similar to those seen in the liver in typhoid fever and other infectious diseases.

We must, therefore, believe that the presence of these soluble poisons in the circulation constitutes a very important feature of diphtheria. These toxins, as already noted, are elaborated in the local lesions of the mucous membranes, and not by the bacteria that may be present in the various viscera. The quantity and quality of the toxins generated seem, as a rule, to be proportionate to the severity of the local process.

Research showing that diphtheria toxin, when introduced into the body, acts as a cell stimulus causing a depression of functional activity.

These changes are definite, and the same qualitatively as those produced by other forms of depressant stimuli. This is probably not due to the action of the toxin directly.

With fatal doses of toxin, the depression varies directly with the

length of time that the toxin is allowed to act upon the tissues. The profound depression which is induced in the tissues is sufficient to account for the accompanying paralysis. Simmons (*Jour. of Med. Research*, July, 1917).

**Catarrhal Diphtheria.**—As we have already seen, the local effects of a diphtheritic inflammation vary greatly.

In catarrhal diphtheria there is redness and some swelling of the mucous membrane of nose, throat, tonsils, or larynx, usually with an increased secretion of the mucous glands. None of these would show macroscopically in the rare cases when death follows such a process. Oertel has, however, found in these cases degeneration of the epithelial cells of the mucous membranes similar to those seen in pronounced cases of diphtheria.

**The Diphtheritic Membrane.**—The membrane is most frequently seen upon the tonsils, soft palate, uvula, pharynx, nares, larynx, trachea, or bronchi. In severe cases it may appear upon the lips, especially at the angles of the mouth, the buccal mucous membrane, and the tongue. Very rarely it appears in the esophagus, stomach, or intestines. In fact, the freedom of the esophagus, when the diphtheritic membrane may be seen completely covering the pharynx and tonsils and extending throughout the whole respiratory tract even to the terminal bronchi, is most remarkable. Even in the severest cases the membrane usually stops abruptly at the beginning of the esophagus.

It is also possible to observe a true diphtheritic membrane upon abraded cutaneous surfaces; upon wounds, as in tracheotomy, or upon the conjunctiva or the genital mucous membrane. The color of the membrane may be white,

gray, greenish white, yellow, or more or less black when there has been hemorrhage from the affected surfaces. It may be thick and elastic, so as to be stripped off in sheets, or thin and diffuent. The thicker membrane is observed upon the surfaces covered with columnar epithelium, with a definite basement membrane, such as the nose, larynx, trachea, and bronchi. Here, too, it is but loosely attached; so that it is often thrown off in casts during life, or after death may easily be stripped off from the underlying surfaces. Upon the tonsils, pharynx, uvula, and fauces, where the epithelium is of the squamous variety and without a basement membrane, the diphtheritic membrane is much more closely attached. Often in these situations we see, after death, no distinct membrane, but a diffuent exudate, which may be easily washed off, leaving a distinctly ulcerated surface beneath.

Microscopically the membrane or exudate is found to consist chiefly of fibrin, mingled with epithelial cells from the mucous membrane; pus-cells, red blood-cells, granular material, and bacteria. The superficial parts of the membrane are granular in character, while beneath we find a more or less distinct network of fibrin, inclosing within its meshes the cells, granular material, and bacteria. The bacteria are the diphtheria bacilli together with streptococci or staphylococci, and rarely pneumococci. The inflammatory process may be superficial or may extend irregularly into the mucous membrane, in some cases involving the submucous tissue and even the muscular coat. The bacteria may likewise penetrate deeply into the tissues, but are usually most abundant in the superficial parts of the membrane. The epithelial cells of the mucous membrane undergo

degeneration, their protoplasm becoming granular, their nuclei fragmented, and the cells ultimately breaking up into granular material. The pathological process is, therefore, a coagulation necrosis involving the mucous membrane more or less deeply.

The pseudomembrane is cast off in masses or is gradually disintegrated, with more or less destruction of the mucous membrane. The process of separation is usually attended by a more abundant cellular exudation beneath the pseudomembrane. Except in the gangrenous cases apart from the tonsil, in which there may be extensive destruction of the tissues, the integrity of the mucous membrane is completely restored, leaving no traces of the preceding disease. Gangrene is not properly a part of the diphtheritic process, but is caused either by especially unfavorable conditions affecting the vitality of the patient or by the invasion of unusually virulent bacteria other than the diphtheria bacilli, probably the streptococci.

The seat and distribution of the membrane vary greatly in different cases. The point of importance with reference both to symptoms and prognosis is the involvement of the larynx. Of 1000 cases analyzed by Lennox Browne, the larynx was involved in 159, in only 4 of which number was the affection limited to the larynx. In a similar analysis of 109 cases by Holt, the larynx suffered in 46, in 10 of which the disease involved either the larynx or the larynx with the trachea or bronchi. Holt gives no purely nasal cases in his series; 2 are given by Browne. In the great majority of cases the membrane is found upon the tonsils or the adjacent parts, the pharynx, uvula, and pillars of the fauces. Six hundred and seventy-two of Browne's 1000 cases showed such distribution.

Since extension of the membrane usually increases the severity of the case and the probability of death, the clinical records of Browne show the comparative frequency of the various forms better than tables which are largely formed from autopsy records. Laryngeal cases are also much more frequently met with in children's hospitals or asylums than in dispensary or private practice.

In cases involving the nasal cavities the process is often catarrhal, and there may be no macroscopic lesion after death. In many such cases, however, there may be membrane in the rhinopharynx, the adenoid tissue of the vault of the pharynx being a favorite seat of the disease. When membrane is developed in the nose, it is usually thick and but loosely attached; so that it may readily be thrown off as casts of the nares.

Upon the tonsils the membrane may be found only in the crypts, resembling a follicular tonsillitis, or it may be in scattered patches, or may completely cover the surface. It is closely adherent. The tonsils are swelled and may even meet in the median line. In most cases the membrane spreads to the surrounding parts: the pharyngeal walls, the fauces, or uvula. The epiglottis is also frequently involved in these cases, even when the larynx is not affected. The membrane often extends into the rhinopharynx and thence may pass to the Eustachian tubes and the middle ear. Upon the uvula or fauces the membrane is usually thicker and more loosely attached than that upon the tonsils.

The uvula is swelled and edematous. The epiglottis, if involved, is swelled and thickened, and one or both surfaces may be covered with membrane. After death the membrane upon these parts

does not show as clearly as during life, and we are apt to find a more or less marked ulceration of the parts. The epiglottis frequently shows considerable destruction of the mucous membrane.

cases where the membrane appears upon the pharyngeal walls it will be found to stop short at the level of the cricoid cartilage, the esophagus being perfectly normal.



Diphtheria of tonsils, larynx, trachea, and bronchi. At upper end the tonsils and base of tongue are seen. The tonsils showed superficial ulceration, covered by thin membrane. Epiglottis is thickened. Right ventricle of larynx filled by exudate and obliterated. From left vocal cord hang some shreds of membrane. Immediately below vocal cords membrane completely covers larynx and trachea. Lifted on the skewers it contracts to a rope-like strand, which is seen extending to finest bronchi on right side. Both lower lobes of lungs consolidated by pneumonia.

Microscopically the pathological process may extend deeply into the submucous or even the muscular coats of these parts, but the ulceration rarely extends beyond the superficial epithelium. In

The appearances in the larynx are quite different from those met with in the throat. The laryngeal process may be simply catarrhal, even when there is abundant membrane in the throat and



there have been marked laryngeal symptoms; so that the larynx after death may appear normal, or there may be a slight congestion of the mucous membrane and the vocal cords after death. In other cases we see a finely granular deposit upon the cords and mucous membrane, and the ventricles of the larynx may be filled by a yellowish-white exudate, but there is no distinct membrane. Again, we may see a distinct membrane masking the cords, obliterating the ventricles, and covering the mucous membrane below.

When there is either exudate or pseudomembrane present in the larynx, it is rarely limited to that part, but will be found to extend into the trachea and bronchi, and even the lungs. In the trachea we may see scattered areas of membrane, or the membrane may line the whole extent of the respiratory tract. There is usually a much more distinct membrane in the trachea than in the larynx itself. Upon these surfaces the membrane is but loosely attached; so that it may be coughed up in complete casts of the bronchial tree, or after death may be readily lifted from the underlying tissues (see illustration).

In a series of autopsies upon 87 cases of laryngeal diphtheria made by one of us (Northrup) the distribution of the membrane was given as follows: In 9 cases the membrane extended from the tip of the nose to the finest bronchi; in 6 from the nose to the bifurcation of the trachea; in 17 from the pharynx to the finest bronchi; in 17 from the larynx to the finest bronchi; in 17 from the pharynx to the main bronchi; in 17 in the larynx and trachea; in 3 in the pharynx and larynx, and in 1 in the larynx only. This work was done in the preantitoxin days, and it must be said that in the autopsies made since the introduction of

antitoxin such extensive distribution of membrane is but rarely met with.

Pseudomembrane may be found in the stomach or intestines, but is rarely, if ever, produced in these situations by the action of the diphtheria bacillus; streptococci are usually found. Occurring upon the conjunctiva, the lips, buccal mucous membrane, or the tongue, the diphtheritic membrane does not present any unusual features.

Diphtheria toxin was found by Rosenau and Anderson to produce, in about 66 per cent. of guinea-pigs, round peptic ulcers in the stomach, but that the intestines are not so affected. M. V. Tyrode (Boston Med. and Surg. Jour., Nov. 19, 1908).

Upon abraded skin surfaces or upon wounds—especially the tracheotomy wound in laryngeal cases—the membrane may be pronounced, and is usually reproduced with remarkable rapidity after removal.

Apart from the lesions produced by the diphtheria bacilli at or by extension from the site of inoculation, they appear to produce no other direct effects, although they may be found present in the viscera. Their toxins, on the other hand, produce definite and characteristic visceral lesions. The experimental work of Welch and Flexner, Abbott, and others has served to make known these remote effects of the toxins. In the great majority of cases of human diphtheria, other bacteria, especially streptococci, are present and active besides the specific bacilli; they are mixed infections, and the problem of determining the action of any one organism is greatly complicated. In forty-two autopsies in cases of diphtheria in which the Löffler bacillus had been demonstrated during life, Reiche is reported to have found streptococci and staphy-

lococci in the kidney or spleen, and streptococci alone in 45.2 per cent. Streptococci were found in the kidney in one case which died on the second day, and positive results were also obtained on the third and fourth days. The results obtained by experimental inoculation of the toxins in susceptible animals are, therefore, much simpler and more easily interpreted than examinations of the viscera of fatal cases of human diphtheria. The lesions produced by the toxins are found in the lymph-nodes, liver, kidneys, spleen, heart muscle, the peripheral nerves, and lungs.

Welch and Flexner have shown that these visceral lesions are produced either by injections of pure cultures of the diphtheria bacillus or by inoculation of their toxins.

The lymph-nodes—cervical, bronchial, mesenteric, axillary, and inguinal—are found to be swelled. There are hemorrhages either beneath the capsule or into the substance of the glands. The cells show more or less advanced degenerative changes both in their nuclei and in the cell-protoplasm. The nuclei are fragmented; the cell-bodies are converted into a finely granular, reticulated material, apparently fibrinous. Similar changes are observed throughout the lymph-structures of the body, Peyer's patches, solitary and agminate follicles of the intestines, etc. The changes in the lymph-nodes rarely lead to suppuration.

The spleen is swelled and usually softened. There may be hemorrhages beneath the capsule or into the substance of the organ. The follicles are enlarged, and the cells show degenerative changes similar to those seen in the lymph-nodes. The liver shows hemorrhages either upon its surface or within its substance. There may be an advanced fatty degen-

eration of the liver. There are also found minute areas in which there has been produced a necrosis of the liver-cells, the nuclei being fragmented or having completely disappeared, while the bodies of the cells show advanced degenerative changes. Some of these areas are infiltrated by leucocytes. Similar focal necroses in the liver have been observed by other poisons than the toxins of diphtheria.

The changes in the kidney include a degeneration of the epithelium of the tubes and glomeruli and hyaline alteration of the glomerular capillaries and smaller arteries. The severe affections of the kidney, acute exudative or diffuse nephritis, met with as complications of the later stages of the disease, are attributable rather to the accompanying streptococcus infection than to the diphtheria itself.

The heart shows a fatty degeneration of its muscles, sometimes so advanced as to produce changes in every fiber. The nuclei of the muscles may also be fragmented.

One of the most striking and constant histological changes in the organs of patients dying of acute diphtheritic toxemia is an extensive fatty degeneration of the muscle of the heart and the diaphragm. These changes were found both in human cases and in animals killed by doses of diphtheria toxin. These changes are rarely detected macroscopically, but microscopically are visible as fine medium-sized or coarse droplets, filling the cells. Dudgeon (Brain, part cxiv, p. 227, 1906).

The two chief cardiac lesions in diphtheria are the parenchymatous and the interstitial. Fatty degeneration is extremely frequent, varying widely in degree and always accompanying the severer lesions. It may occur at any time in the disease. A much severer degeneration, both focal and general, which affects all parts of the muscle-

fiber, the contractile elements, the protoplasm and the nucleus, and which leads to the formation of granular detritus and large irregular hyaline masses, also occurs. This is only found late in the course of the disease, rarely earlier than the seventh day. The interstitial changes are of two types. In one there are focal collections of lymphoid and plasma cells. In the other there is invasion of the degenerated and necrotic muscle cells with endothelial cells and polymorphonuclear leucocytes. These are all essentially late changes. Only fatty degeneration is seen before the sixth or seventh day. The early circulatory disturbance is extraordinarily severe, but, thanks to antitoxin, is rarely seen at present. Romberg's and Passler's experiments show that this is due to failure of the vasomotor center, though undoubtedly the heart itself is affected. The late circulatory disturbances may appear at any time from the second to the fifth week. The first symptoms are usually to be found in the pulse, which drops with the temperature, often to below normal, remaining there or rising and falling again. In a certain percentage of cases it may be persistently high, but either of these means almost certainly myocarditis. At other times the first symptom is irregularity in the force or rhythm and the former is constantly present and may last for months. The worst prognosis is given in cases with lower and constantly falling rate. Heart examination reveals the same abnormalities together with murmurs and evidences of dilatation, and here the personal equation of the examining physician has played a considerable part in their interpretation. Accurate deductions cannot be drawn at present as to the severity of the lesions from the murmurs, and it is the author's personal opinion that dilatation has been diagnosed too frequently, though it would be wrong to say that it is unusual.

A sign of mild cardiac disease of greater value on account of its constancy is the alteration in character

of the first sound of the heart, consisting in the more or less complete disappearance of the muscular element of the first sound, making it weak and short, and what is usually called "valvular" in quality. Studies in regard to blood-pressure are incomplete and unsatisfactory. It is generally somewhat subnormal and when below 75 mm. always means a serious condition and below 70 mm. great danger. A progressive fall should excite more concern. General symptoms, such as pallor, apathy or irritability and vomiting, are often much in evidence. Loss of weight is common even in convalescence. The cause of death has not been determined by experiment, but the clinical evidence is conclusive that it is due to myocarditis. J. Howland (Jour. Amer. Med. Assoc., Dec. 19, 1908).

Case of diphtheria, with full heart block. The *a-v* bundle and node were found by the authors to be involved in an acute inflammatory process, and similar lesions were present in the *a-v* bundle in a case of malignant endocarditis in which conductivity was defective. In 3 cases of acute endocarditis, with nodal rhythm, the *a-v* node was acutely inflamed, the bundle being only and but slightly affected in one instance. Cowan, Fleming, and Kemaedy (Lancet, Feb. 3, 1912).

The arrhythmias of diphtheria are not only of great variety, but vary from moment to moment, and it is possible to trace in them the whole gamut of progressing and retrogressing disturbances in conduction of the impulse. Only polygraphic methods, with radioscopy, suffice. Writer describes the case of a boy of 14 with diphtheria for 8 days before antitoxin was given. Traces showed heart block and extrasystoles. Patient succumbed the twenty-fifth day to weakness of the myocardium. The lesions in the latter were both interstitial and parenchymatous, but they were less pronounced in the bundle of His than elsewhere. Aviragnet, Lutembacher and Le Soudier (Arch. des mal. du cœur, etc., June, 1918).

The blood shows a leucocytosis which is greatest during the height of the disease and decreasing during convalescence. The polymorphonuclear cells are chiefly affected by this increase. Myelocytes may be found in the peripheral blood, this being especially true in the severe cases, and they may range from 3 to 16 per cent. of the total white cells. There seems to be some relation between the severity of the infection and the degree of leucocytosis, but the leucocyte count is of little value from a standpoint of prognosis.

Condition of leucocytes in diphtheria, before and after administration of **antitoxin** in 13 cases of clinically undoubted diphtheria. The writer found that diphtheria is attended by a varying degree of hyperleucocytosis, usually moderate. Occasionally hyperleucocytosis may be absent in extremely toxic or extremely mild cases. The differential counts in the leucocytoses of diphtheria show proportions of polymorphonuclear and mononuclear cells consistent with the grade of leucocytosis. In these leucocytoses the eosinophiles are present in unusually small numbers, and the myelocytes, basophiles in moderately small numbers. Neither the degree of leucocytosis nor the proportions of any of its constituent types of cells indicate, except within very broad lines, the severity of the infection or the outcome of the disease. The administration of **antitoxin** has no appreciable effect on the degree of the leucocytosis, the proportions of its constituent types of cells, or the staining reactions of these cells in dry preparations, stained either by Wright's method, Ehrlich's triacid mixture, or hematoxylin and eosin. Karsner (Univ. of Penna. Med. Bull., Sept., 1908).

The changes produced in the brain-cells of animals inoculated with diphtheria toxins have recently been made the subject of study (Carlo Ceni; Berk-

ley). Swelling of the processes of certain cells of the brain with some minor changes in the conformation of the cells, but without evidence of degeneration of the cells or their processes, was observed. The cerebral were more affected than the cerebellar cells.

Various lesions have been found in the spinal cord in cases of diphtheritic paralysis, but none of the changes observed in the cord have thus far been accepted as the explanation of the paralysis.

Katz has recently reported finding, after careful examination of the cords of 3 fatal cases, distinct changes in the motor ganglion cells of the anterior horns of the cord. The changes were either a fatty degeneration affecting the cells or complete death of the cells with all processes, and especially the axis-cylinder. All ganglion cells of the cord were similarly affected, but not so markedly as the motor cells of the anterior horns.

The changes in the peripheral nerves, on the other hand, are looked upon by some as the most characteristic pathological lesion of diphtheria. The affected nerves are sometimes red and swelled, from congestion and edema, but the degeneration of the nerve-fibers is the characteristic feature of the process. Single nerve-fibers or a whole nerve-trunk may be affected. The changes may be either interstitial or parenchymatous. In the parenchymatous form there is usually a more or less marked infiltration of leucocytes within the nerve-sheath, between the sheath and the nerve-fibers, or between the fibers themselves. The medullary sheath of the nerve-fiber is swelled, undergoes a fatty degeneration, and may altogether disappear. The axis-cylinder undergoes a similar degeneration; it may be

changed to a granular mass and be completely absorbed. The empty sheaths of Schwann may be the only evidence left of the former nerve-fiber. Sooner or later the degeneration stops; regeneration begins and usually results in complete restoration of the nerve-fibers. In the interstitial form the increase of the connective tissue of the endoneurium and perineurium is the marked feature of the process. In some cases the changes are both parenchymatous and interstitial.

The pulmonary changes produced by the experimental action of diphtheria bacilli or their toxins are slight and of no importance, but the pulmonary complications of clinical diphtheria are frequent, severe, and of great moment. Wright, More, Kanthack, Stephens, and others have demonstrated the presence of diphtheria bacilli in the lungs in fatal cases of diphtheria, but the presence of the bacilli apparently has but little to do with the production of pulmonary complications. In 1889, in an investigation of a series of 17 cases of pneumonia complicating diphtheria, Prudden and Northrup found streptococci both in the pseudomembranes in the throat and in the lungs. It was further shown that the inoculation of streptococci in susceptible animals served to produce changes in the lungs similar to those seen in clinical diphtheria. These observations have been fully corroborated, and the streptococci are accepted as the active agents in the production of the pneumonia which so frequently complicates diphtheria. Bronchopneumonia is met with in the great majority of fatal cases, especially in hospital practice. In the most acute cases we find the posterior parts of one or both lungs deeply congested, firm to the touch, and on section showing scat-

tered areas of peribronchial consolidation, deep red in color. The lower lobes are usually more affected than the upper. In the slower cases we find the areas of pneumonia scattered throughout both lungs, but affecting the lower and posterior portions especially, the consolidation often involving a large part of both lungs and on section appearing mottled, reddish brown, and yellowish white. Pleurisy and empyema are rarely met with. In laryngeal cases with marked stenosis there is usually emphysema, both vesicular and interstitial. The interstitial emphysema may involve the cellular tissues of the neck and even extend over the trunk.

**PROGNOSIS.**—In no other acute infectious disease is the prognosis so uncertain as in diphtheria. Many factors must be considered in determining the prognosis in any given case:—

1. Age of the patient. Happily, children under 6 months of age are rarely attacked; but between that age and 2 years many cases are seen, and the mortality is often frightful. With increase in age the mortality falls steadily, but even in adult life diphtheria may readily prove fatal.

The following tables, taken from the article of Biggs and Guerard in "The Use of Antitoxic Serum," show the favorable influence of age very clearly:—

Herz: Mortality Percentage.

0-1 year .....	80.00
1-3 years .....	45.00
3-5 years .....	40.00
5-10 years .....	17.00
Over 10 years .....	17.00

Baginsky: Mortality Percentage.

0-2 years .....	63.3
2-4 years .....	52.8
4-6 years .....	37.9
6-10 years .....	24.6
10-15 years .....	14.6

## Hirsch: Mortality Percentage.

0-1 year .....	83.3
1-3 years .....	82.5
3-4 years .....	63.9
4-5 years .....	46.9
6-7 years .....	43.2
Over 7 years .....	22.2

The ratios are all derived from cases treated previous to the introduction of antitoxin or without its use. The analysis of a large number of cases treated by antitoxin, while the mortality ratios are diminished, shows that the age influence remains practically the same.

Age.	Cases.	Deaths.	Mortality percent-age.
0-2 years .....	1494	469	31.4
2-5 years .....	3678	762	20.7
5-10 years .....	3184	473	14.8
Over 10 years .....	1444	99	6.9

Of 265 patients with phlegmonous diphtheria admitted to the Children's Hospital at St. Petersburg from 1895 to 1908, 67 died during the first day. The mortality decreased with the age, from 100 to 16.6 per cent. Early vomiting is an unfavorable sign, generally being followed by paralysis of the heart. Nephritis was observed in nearly all the cases from the first, but it proved mild. Under **antitoxin** the throat cleared by the beginning of the second week, but the heart symptoms generally developed at this time. Blumenau (Archiv f. Kinderheilkunde, Bd. lv, Nu. 5-6, 1911).

2. The site of the disease. Involvement of the larynx either primarily or secondarily adds greatly to the danger of the case. The large death rate under 2 years is due, in great part, to the strong tendency of the disease to invade the larynx during that period.

The use of **antitoxin** has materially changed all the figures relating to the fatality of the various forms of diphtheria, but the laryngeal process remains the most deadly.

3. The time of beginning treatment. In the use of antitoxin it has been dem-

onstrated beyond the shadow of a doubt that, the earlier the remedy is employed, the surer is recovery, while after the fifth day the remedy exerts little or no influence.

It has always been quite evident that delay in undertaking treatment led to unfavorable results, but the vital necessity of promptness has been impressed upon us by the overpowering evidence afforded by the results obtained when antitoxin is resorted to early in the case.

The high mortality from this disease in the United States is due to the following factors: 1. Late diagnosis, late or inefficient prophylactic measures, lack of faith in **antitoxin**, and insufficient dosage in serious cases. 2. Cases diagnosticated early demand from 3000 to 5000 units immediately, to be followed by a further administration of 5000 units or more in from four to six hours if there is no improvement. Cases diagnosticated late should receive from 10,000 to 30,000 units immediately, repeated at intervals of four to six hours until there is a complete subsidence of symptoms. Hill (Med. Rec., April 1, 1911).

There has been much variability and uncertainty as to dosage and the aim appears to be to give exceedingly large doses. In truth there are seldom present at one time more than 100 units of toxin even in the most severe cases, and 1000 units of antitoxin given *intravenously* has an equal effect to 20,000 units given under the skin. The Schick reaction aids in the appreciation of the effects of antitoxin. A single dose of antitoxin should be sufficient. W. H. Park (Boston Med. and Surg. Jour., Aug. 26, 1915).

In an epidemic of diphtheria in Basle all the recovered children received their antitoxin either early (pharyngeal cases 2.5 days) or late (nasal cases 20 days). The dead children did not receive serum until an average of more than 6 days had expired; while in children who recov-

ered from laryngeal diphtheria the interval was but 2.3 days. It is very rare for death to occur in diphtheria when the membrane has been expelled in the first 2 or 3 days, and this result is seen when antitoxin is given early. Serum sickness in the form of a rash was seen 12 times, while anaphylactic phenomena were absent. Massini (*Correspondenzbl. f. Schweizer Aerzte*, Mar. 2, 1918).

4. The degree of toxemia. This feature is usually developed in proportion to the lapse of time from, and the severity of, the onset of the disease. It may be slowly or rapidly developed, and in many cases apparently mild in the beginning we may later see the severest types of toxemia.

5. The extent of the membrane and the rapidity of the extension.

6. The presence of complications, especially from bronchopneumonia or nephritis. The pneumonia of diphtheria is by far the most important of the complications. The late onset of the cardiac complications of diphtheria is to be remembered. No case of severe diphtheria can be considered altogether out of danger for some weeks after apparent recovery.

7. The surroundings of the patient. The mortality of diphtheria is considerably greater in hospitals or asylums for children than in private or dispensary practice. The crowding of the children together seems to exert a very unfavorable influence by exposing them to danger from complications, and most especially to pneumonia.

The frequency and gravity of diphtheria has increased during the last 2 years in Rome. Substandard children, especially those with congenital syphilis and tuberculosis, are especially liable to it. The early use of antitoxin in large doses and intubation have kept

the mortality at 16 per cent. Ritossa (*Pediatria Arch.*, 1, p. 330, 1925).

8. The mortality of diphtheria may vary greatly from year to year in the same place or in different epidemics, the causes of the variation not being apparent.

Such variations in the type of the disease may properly be taken into account in the prognosis of individual cases.

There are certain cases of diphtheria in which a fatal ending can with certainty be predicted. The symptoms presented by these patients are as follows: 1. A grayish color of the face, which in addition presents an anxious expression. 2. Vomiting. This seems independent of food and is not accompanied by nausea. It presents a similarity to cerebral vomiting. The vomited matter is yellow or green. 3. Abdominal pain. This is sometimes very severe. It is, however, nearly always present in these cases. It is referred to the umbilicus. No abdominal tenderness can be elicited. 4. Albuminuria. This is generally present and often to a large amount (from one-sixth to a quarter). There are no tube casts. 5. Suppression of urine is the rule in these cases. 6. Alteration in the rhythm of the heart sounds. This appears after the vomiting has set in. One of the sounds of the heart is reduplicated, thus giving an imitation of the sounds to be heard when a horse gallops. The patients are generally very restless and consciousness is maintained until the end. The membrane on the throats in these cases is dark colored and the smell of the breath is most offensive. In 6 cases antitoxin had no effect, though 6000 units were generally given. Harris (*Lancet*, Sept. 28, 1907).

Systematic investigation of the planar reflex in cases of diphtheria. The occurrence of Babinski's sign in diphtheria was first recorded by Kiroff in 1905, and since that time the writer has drawn at-

tention to its frequency in association with precocious paralysis of the palate and with hemorrhagic diphtheria. He now records his observations on 877 cases of the disease in which he has examined the state of the plantar reflex. An extensor response of the great toe, with varying movements of the other toes, was found in 172 cases—that is, in 19.6 per cent.; in 29 flexion alternated with extension, and in 676 the normal flexor response was obtained. It occurs in the acute stage and is replaced by flexion during convalescence. It is more frequently observed in the severe forms of diphtheria than in the mild ones, and its occurrence may have a certain prognostic value, although it is not of such grave omen as precocious paralysis of the palate. J. D. Rolleston (*Review of Neurol. and Psych.*, July, 1910).

**PROPHYLAXIS.**—In typical diphtheria we have to deal with an acute infectious disease in which we now know the nature of the contagion and its ways of spreading. The bacilli present in the nose or throat of the patients are the active agents, and anything which may, either directly or indirectly, be contaminated by the discharge from the affected surfaces may be the means of communicating the disease to others. The first step in prevention is, therefore, the **isolation** of the diphtheria patient. Suspected cases should be isolated as thoroughly and promptly as those in which the diagnosis is settled. It is to be remembered that during epidemics or in any case of exposure many of the mild cases of “sore throat” are, in reality, diphtheria, and should be treated as such in this respect.

Moreover, as has previously been noted, diphtheria bacilli may be found in the throats of those who, although perfectly healthy, have been exposed to infection, these constituting the **carriers**. This is especially true of chil-

dren, and in families where diphtheria is present the well children should be kept from attendance at schools or like gatherings, where they may possibly convey the disease to others more susceptible than themselves. In the course of epidemics it is often necessary to close all schools before the ravages of the disease can be controlled. A number of measures have been proposed to rid the carriers of these contaminating germs, but so far none has proven absolutely dependable.

**Active Immunization by Injections of Mixed Toxin and Antitoxin.**—Von Behring has worked out a method by which a prolonged, active immunity to diphtheria may be produced. It consists in injecting a combination of diphtheria toxin and antitoxin so proportioned that upon administration to guinea-pigs the antitoxin almost or quite offsets the poisonous action of the toxin. In human beings such a mixture, though bringing about prolonged immunity, causes only a slight reaction, provided the system has not already become over-sensitive to diphtheria bacilli.

An important additional result is that in patients sensitive to horse serum a passive immunity can be produced by injecting antitoxic serum obtained from human beings; furthermore, this immunity will not rapidly disappear, as would be the case were horse serum used, but will persist as long as the active immunity obtained with the toxin-antitoxin mixture, owing to the fact that the material introduced is derived from an individual of the same species.

Children from 4 to 15 years old are almost always more sensitive than the newborn to the toxin-antitoxin mixture. Thus, with a dose which in a newborn infant would cause



practically no reaction, it was found that in an older child the same amount ( $\frac{1}{16}$  c.c.) caused an intense febrile reaction, with the active production of antitoxin by the body to the extent of 600,000 units. Since this is far in excess of the intensity of immunity required for practical purposes, there is ample opportunity for producing a sufficient degree of protection without inducing a marked reaction. In the child referred to it was calculated, from several observations of the antitoxic power of the blood, that it would take over two years before this power would diminish to a level which is attained with the ordinary passive immunization by diphtheria antitoxin in ten days.

The toxin-antitoxin mixture used must be free of aerobic and anaerobic germs, and must be non-toxic in guinea-pigs in the dose of 0.0005 Gm. for every 100 Gm. of body weight. Infants are to be given 0.0001 Gm. as the initial dose, and older children only 0.0005 Gm., injected under the skin in 0.001 Gm. of fluid. The classes of subjects to be inoculated are those exposed to diphtheria in hospitals, schools, and buildings occupied by several tenants; well persons, not exposed to diphtheria at the time, in orphan and insane asylums, prisons, etc., and diphtheria carriers—the latter being usually very sensitive to the remedy and developing a high degree of immunity. In beginning cases of diphtheria and in persons with a weak heart and irregular pulse the mixed inoculations are not at present to be tried. Von Behring (*Semaine méd.*, May 7, 1913).

In 1915 Park wrote that the 30 years then passed had witnessed the growth and decay of the hope that by isolation and terminal disinfection the incidence of diphtheria might be reduced. The total mortality was just as high as ever (1915). Passive immunity protected for a few weeks; 1000 units of antitoxin conferred immunity for about 3 weeks. Its short duration led to efforts to increase it. Behring used a toxin-antitoxin mixture for this purpose. Such mixtures were useful in speeding and increas-

ing the antitoxin yield of horses. Theobald Smith suggested and Behring applied it. By 1918 Park was able to announce that results obtained in the preceding 3 years had made it possible to immunize the child population against diphtheria.

The dose of **toxin-antitoxin** mixture given is generally 1 c.c., injected 3 times at intervals of 1 or 2 weeks. In about 85 per cent. of susceptible individuals this procedure causes the subject to yield a negative Schick test and become immune. This immunity develops only in 1 to 6 months after the injections, but in at least 90 per cent. of children it lasts more than 6 years.

All infants below 12, and if possible below 18 months of age should be actively immunized with 3 doses, each 1.0 c.c., given subcutaneously, of **toxin-antitoxin**. These injections should be given irrespective of the Schick test the infants may show at the time of immunization. The injections are given subcutaneously in the arm or below the angle of the scapula, and repeated every seven days. The toxin-antitoxin is well tolerated by young infants, and for that reason the dose advised is the same as that given to older children. The relatively larger dose of toxin-antitoxin will, of course, also give rise to a better immunizing response. All children over 18 months of age, as well as all youths and adults, should be tested with the Schick reaction first, and only those giving a positive reaction immunized with toxin-antitoxin. In infants below 18 months of age the Schick test is not a necessary part of the immunization, since all the infants should be actively immunized. The toxin-antitoxin mixture should be prepared in a reliable laboratory and carefully tested for potency in the guinea pig before it is sent out for use. The mixture used should be slightly toxic and should represent about 85 per cent. of a lethal plus to each unit of antitoxin.

The active immunization against diphtheria should be carried out first of all by the private physicians in the different homes, where a majority of the infants can be reached.

In larger centers of population the milk stations, day nurseries, children's dispensaries, infant and orphan asylums furnish large groups of children suitable for immunization. The children of pre-school age found in kindergartens and those of school age should be tested first with the Schick reaction, and those giving a positive test actively immunized.

Adults, especially those frequently or constantly exposed to diphtheria, such as physicians, nurses, hospital orderlies and patients in contagious disease hospitals, should likewise be tested for the Schick reaction.

All those giving a positive reaction should be actively immunized. Zingher (*Amer. Jour. of Dis. of Children*, Aug., 1918).

The **Schick test** makes it possible to ascertain when a person is immune. This particularly applies to infants and young children. In older people, however, it may be found that some toxic substances in the broth injected cause a pseudoreaction, but with practice most of these can be determined. Zingher found from studies on children extending over years that in only 3 per cent. of the children did a negative Schick test change to a positive test. A negative Schick therefore means an immunity for years, and, the writer believes, for life.

Occasionally there are gross discrepancies in the Schick test, due to imperfect toxin or methods. Infants obtain their immunity from their mothers, and from infancy on to 2 years this immunity disappears, so that the greatest number of non-immunes occur in infants between the second and third years, and from then on the percentage of non-immunes grows less as ages advance. The **toxin-antitoxin mixture** is used on the non-immunes. It has strong immunizing properties, and has been given to infants one week old in full adult doses with no deleterious effects. After one injection 70 per cent. will be immune at the end of 1 month; 2 injections will give about 90 per cent. of immunes, so that by reinjection

most of the non-immune can be rendered immune.

Babies stand the immunizing doses better than adults and older children, in whom more marked reactions occur, with rise of temperature, prostration, etc. It is therefore believed that the babies between 6 months and 2 years should be the ones to be immunized, and an immunization of the whole infant population could thus be obtained. The method is entirely harmless, gives permanent immunity, and would eliminate diphtheria. Park (*Trans. Med. Soc. State of N. Y.*; *N. Y. Med. Jour.*, Jan. 29, 1921).

The writer gave 100 Schick-positive children **toxin-antitoxin** mixture by the mouth, and found that after this procedure (how long after is not stated), 91 of these children were Schick-negative. But it appears that this immunity is retained for a short period only. Pockels (*Klin. Woch.*, July 23, 1925).

Park (*Jour. of the Med. Soc. of New Jersey*, July, 1924) used a preparation very rich in toxin, *i.e.*, 140 fatal doses for a guinea-pig and an equivalent amount of antitoxin to make it nearly non-toxic; but it caused sore arms and marked local reactions. Two or three per cent. of the children and more adults showed a rise of temperature, and at times were unable to work a day or more. This led to a great reduction of the activity of the toxin-antitoxin ( $\frac{1}{30}$ ), the resulting mixture being thereupon generally used in this country.

Hooper, of Boston, tested a number of people who had received doses of toxin-antitoxin preparation, but found that a year later, some of them, especially when they received an injection intracutaneously of horse serum, gave a reaction of sensitization. Even a minute amount of horse serum in sensitive individuals would cause sensitization in about 20 per cent. That this fact is not of real practical importance is probable, for at the Willard Parker Hospital children were injected after intracutaneous tests without any regard to the reaction, and no marked ill effects have been found. They showed a reaction about the size of a 25-cent piece, which constituted a vulnerable feature of toxin-antitoxin. It was then suggested that if goats were used as a source

of toxin-antitoxin, there would be no sensitization of human beings to horse serum.

A. Zingher (N. Y. State Jour. of Med., Feb. 1, 1924) has described a **new toxin-antitoxin mixture** containing only a  $\frac{1}{10}$  L+ dose of toxin per cubic centimeter instead of the 3 to 5 L+ in the old-type mixtures. The toxic or underneutralized fraction of the toxin-antitoxin remains the same as before. Local and constitutional reactions from the new mixture are less, and it can be given to older children and adults without fear of marked local disturbance. Three doses of 1 c.c. each are given at intervals of 7 to 10 days, preferably intramuscularly in the arm.

Cattle may be used instead of horses in the production of diphtheria and tetanus antitoxins. In many children treated with such serums, the incidence of serum sickness was somewhat less than with antitoxin from horses. Kraus, Cuenca and Sordelli (Semana med., Mar. 24, 1921).

Both the new toxin-antitoxin and anatoxin have given good immunizing results in the cases seen by the authors, with but slight reactions. Anatoxin contains no horse serum to cause sensitization, but substitution of goat antitoxin for horse antitoxin will likewise obviate this difficulty, and this change is now being made. This would remove the fear created by the recent experience with frozen toxin-antitoxin in which the freezing sets free the toxin, with resulting severe local and constitutional reactions. Park and Zingher (Amer. Jour. Dis. of Childr., Oct., 1924).

**Anatoxin.**—G. Ramon (Paris méd., Dec. 6, 1924), of the Institut Pasteur, discovered and introduced in 1924 a new immunizing material to which he gave the above name, based on his observation that mixtures of fresh diphtheria antitoxin and toxin undergo flocculation when mixed in such relative quantities as neutralize each other, and that the power of a toxin to induce immunity is proportionate, not to its actual toxicity, but to its flocculating property. By certain procedures, in particular by adding 3 or 4 parts of formaldehyde solution to 100 parts of toxin and incubating at 40° C. for 1 month, the toxicity of the toxin can be made almost

to disappear, while its flocculant and immunizing properties remain unimpaired. Aside from its low toxicity, anatoxin is advantageous in being stable; it is unaffected by a temperature of 70° C. or by being kept in the ice-box or at room temperature for 1 year. Two injections of 0.5 and 1 c.c., 1 to 2 weeks apart, induced immunity in 90 to 95 per cent. of cases in 5 to 6 weeks, and in 100 per cent. in 2 months. It is believed the immunity will usually persist throughout life. Anatoxin also has possibilities as a therapeutic agent, in the treatment of carriers, in the prevention of late complications, and in the rapid, intense and safe immunization of horses.

The writers found that the immunity conferred with 2 injections of diphtheria anatoxin (0.5 c.c. and 1 c.c.), at 3 weeks' interval, still persisted a year later in 10 children, showing a negative Schick reaction. There was no opportunity during this period for intercurrent contaminations which might have maintained the immunity. The persistence of the immunity is ascribed to the action of the anatoxin and in no way to an occult spontaneous immunization. Lereboullet and Joannon (Bull. de la Soc. méd. des hôp., May 22, 1925).

The writer injected anatoxin twice, with an interval of twenty days, in 108 children. Almost 91 per cent. of them became Schick negative. All the 12 children injected 3 times became negative. Contrary to this, 15 of 43 tuberculous children remained Schick positive after 2 injections. Nasso (Pediatria, Dec. 15, 1925).

A comparative study was conducted in various institutions, affording opportunity for 1297 inoculations. About 275 children, aged from 5 to 18, were vaccinated when no cases of diphtheria had occurred in the institution. Two injections (0.5 and 1 c.c.) were given at an interval of from 15 to 22 days. The Schick test in 231 of these children, 21 to 29 days after the second injection, elicited a negative reaction in 96.1 per cent. and a positive in 3.89 per cent. In another institution, after the occurrence of a case of diphtheria, 163 children were vaccinated twice with a 16 day interval (0.5 and 1 c.c.) and the

dicates that the immunity thus acquired may last for months and years. The method may perhaps be advantageously combined with passive immunization by injection of antitoxin when rapid action is desired. The diphtheria toxin was diluted with twice the amount of salt solution in a later group of 11 children to avoid by-effects, and the tampon was left in the nose only half an hour every third day. Blumenau (*Jour. Amer. Med. Assoc.*, from *Jahrbuch f. Kinderheilkunde*, Aug., 1911).

Increasing the dose of antitoxin beyond a certain point does not further lower the mortality, which, during a recent epidemic, was about 18 per cent. On the other hand, the results of immunization of those who had been or were to be exposed were brilliant. Of nearly 500 so immunized, but 5 developed the disease, and that in a very mild form. Of the small number in which immunization was refused 14 developed the disease, with 3 deaths. Eckert (*Deut. med. Woch.*, Nov. 21, 1912).

At least three weeks of immunity are conferred to a certainty by means of antitoxin; in individual cases it may be prolonged, say up to three and four months. If new cases develop during this period they are extremely mild ones. Braum (*Deut. med. Woch.*, Feb. 6, 1913).

Diphtheria has long been endemic at Mendoza but it has recently been brought under control by systematic use of a vaccine to immunize all in the environment of every case of diphtheria. This seems to confer a more lasting immunity than with the use of antitoxin, while experience indicates that it is free from the drawbacks of the latter. Ponce (*Semana medica*, Buenos Aires, Feb. 28, 1918).

**Isolation of Carriers.**—Recent years have been marked by the establishment in our large cities of a system of inspection by trained physicians of all school-children who present the first symptoms of illness: a progressive step in preventive medicine that can undoubtedly do

much to protect these communities from epidemics of diphtheria. Suspected cases of diphtheria are to be isolated, but should not be put into diphtheria wards or hospitals until the diagnosis is assured. Our reliance must be upon the bacteriological diagnosis, for in case of exposure the mildness of the individual case is no surety that it is not dangerous to others.

These cases call for especial care, both in making and in examining the cultures. With proper methods twenty-four hours usually suffice to settle the question of diagnosis. In case of doubt the isolation of the patient should be continued and the bacteriological examination repeated.

In all our large cities provision is now made for the treatment of diphtheria in special public hospitals. To these hospitals are sent all cases that cannot be properly cared for and isolated at home.

Proper isolation of diphtheria cases developing in hospitals or asylums, especially those for children, is of very great importance, since these institutions contain the most susceptible material for the action of diphtheria bacilli. They should be provided with diphtheria wards, located, if possible, in separate buildings. The isolation of such wards should be complete. In no other way can the inmates of such institutions be protected from repeated outbreaks of diphtheria.

In private houses one or more rooms should be set apart for the use of a diphtheria patient. No one but the patient and the attendants should be allowed to enter the sick-room. All expectoration, bits of membrane, etc., should be received in cups containing a solution of carbolic acid, 1:40, or bichloride of mercury, 1:1000. Instead of handkerchiefs, bits of gauze or old linen

should be used, and burned when soiled. All bedding and clothing used during the attack should be soaked for several hours in a 1:40 solution of carbolic acid and afterward boiled. All eating utensils should be sterilized by boiling. Nothing that has been in the room should be taken from it without subjecting it to sterilization in some way.

The physician in charge of a case of diphtheria before entering the sick-room should cover his clothing by a cotton or rubber gown reaching to the feet and a cap to completely cover the hair. The cap and gown should be kept outside the sick-room and should be sterilized at the conclusion of the case. The physician should remember that, in examining the throat in cases of diphtheria, he stands in great danger of infection by having the patient cough in his face. Many a life has been sacrificed by careless exposure in this way. As a measure of protection, the physician is often advised to have a pane of ordinary window-glass held before the patient's face during inspection of the throat.

Unfortunately, very few men willingly adopt a cumbersome device which at the same time interferes with the examination; but, in case the patient does cough during the examination, the physician should protect himself by thoroughly washing the face and hair with soap and water, and then using a solution of **mercury bichloride**, 1:1000. The hands should always be washed and disinfected on leaving the patient's room.

Nurses caring for diphtheria patients should especially avoid contracting the disease by exposing themselves to the discharges from the nose or throat of the patient. Practically there is no danger from the breath of the patient. The nurse should keep her hands thoroughly clean at all times and should

have a disinfecting solution of **carbolic** or **mercury bichloride** at hand so that she may use it constantly. A cleansing gargle of **normal salt solution**, **Dobell's solution**, or **Seiler's solution** should be used several times a day. It is advisable to administer an immunizing dose of **antitoxin** to all persons exposed to the disease, and 500 to 1000 units are sufficient for this purpose.

If this is not done, **antitoxin** in protective dose should be given at the first sign of a "sore throat."

After leaving a diphtheria case the nurse should thoroughly disinfect both her clothing and her person. It is also customary to require the nurse to allow a period of at least five days to pass after leaving a case of diphtheria before assuming charge of any other patient.

**Length of Quarantine.**—The bacteriological researches of recent years have given us some very definite information bearing on this point. It has already been noted that the bacilli may persist in the throat for weeks after an attack, and that such bacilli have been proved fully virulent. Park reports a series of careful observations upon the time of the disappearance of the bacilli from the throat in 1736 cases of diphtheria. Briefly, he found that the bacilli had disappeared within one week in 3 per cent. of the cases, in one-third of the cases at the end of the second week, in two-thirds at the end of the third week, in four-fifths at the end of the fourth week, and in the remainder the bacilli persisted for varying periods up to 91 days. This last case was one of simple nasal discharge containing diphtheria bacilli, from which both nurse and mother contracted diphtheria. The mildness or severity of the case gives no basis for determining the time that the bacilli may remain in the throat. The

only accurate method of determining the period of quarantine is that of making cultures from the throats. Only when cultures fail to show the presence of the bacilli in the throat or nose can the case be regarded entirely devoid of danger to others. If cultures cannot be employed, we may elect an arbitrary period of three weeks from the disappearance of membrane for the removal of quarantine restrictions. After that time, if the bacilli have not actually disappeared from the throat, they are but few in number, and the danger of communication is slight.

Disinfection of the infected rooms upon the termination of the case should be thorough. The walls and ceilings are to be scrubbed with **mercury bichloride**, 1:1000, or rubbed down carefully with bread: a simple method of removing the clinging dirt and bacteria by mechanical means. The woodwork, floor, and furniture are to be scrubbed with bichloride. The woodwork, walls, etc., are to be repainted or papered anew. Carpets, upholstery, etc., can be disinfected by steam. Clothing, linen, etc., may be boiled. Anything which cannot be disinfected by some of these means should be burned. Books and toys that children have used during their illness should be thus destroyed. Even the most careful disinfection will, in some cases, prove ineffective. The following are the regulations for fumigation established by the New York Board of Health:—

"All the crevices in rooms to be fumigated must be sealed or calked to prevent the escape of the disinfectant, and one of the following disinfectants used in the quantities named:—

"(a) **Sulphur**, 4 pounds for every 1000 cubic feet of air-space, eight hours' exposure.

"(b) **Formalin**, 6 ounces for every 1000 cubic feet of air-space, four hours' exposure.

"(c) **Paraform**, 1000 grains for every 1000 cubic feet of air-space, six hours' exposure."

Mixing commercial potassium permanganate with 40 per cent. formaldehyde solution constitutes a simple means of liberating formaldehyde gas, which calls for no special apparatus. For each 500 cu. ft. of space there are required  $6\frac{1}{2}$  ounces of permanganate and 1 pint of formaldehyde solution. The former is first placed in a tin dish, and the solution then poured over it.

Much may be done to prevent spread of diphtheria by properly caring for children who may be exposed to infection. Catarrhal conditions of the nose and throat undoubtedly afford a favorable soil for the location and growth of diphtheria bacilli. Enlarged tonsils and adenoid growths in the nasopharynx fall in the same category. All such conditions should be carefully treated.

Healthy mucous membranes are always a safeguard against attacks of diphtheria.

**GENERAL MEASURES.**—First of all, the sick-room should be well lighted and ventilated. Care in this respect is especially necessary in children's hospitals. Crowding a number of cases of diphtheria together in one ward is undoubtedly harmful. It is much better to have a number of small wards, accommodating three or four patients, than one large one in which all are assembled together. Cases in which pneumonia has developed should not be kept in the room with those still free from it. Attention should be given to **feeding** the patients, as the best means of enabling them to bear the attack of the disease upon the vital powers. Us-

ally, on account of the soreness of the throat, fluid foods can be best taken, but semisolids can be given in some cases. Our chief reliance must be upon milk. It should be given at regular intervals, every two hours, and in such quantity as the patient will take. There is little danger of over-feeding. The difficulty is usually to get the children to take sufficient nourishment. In addition to the milk, we may give beef-juice, beef-tea, or thin gruels. In children that have been intubated semisolids can sometimes be taken better than fluid nourishment. Bread and milk answer the purpose in such cases.

Nursing children should be fed with milk drawn by a breast-pump. In this way the children are saved the exertion of suckling and the mothers are protected from the danger of infection.

In septic cases the children often refuse food altogether or vomit it immediately it is taken. They may then be fed by the stomach-tube. If the tube cannot be passed through the mouth, we can usually succeed in passing it through the nose. This method may also be employed in intubated cases where the attempt to swallow food is followed by violent coughing or choking.

Rectal feeding with peptonized milk is a last resort, and seems to be of little value in children.

**Rest** in bed is an essential feature of proper treatment. Whatever handling or interference is required should be so arranged as to tax the patient as little as possible. Zeal for thorough local treatment has often led to fatal excitement and exertion on the part of the patient. Especially in cases of cardiac weakness should absolute quiet be enjoined, and all treatment that tends to excite the child or cause it to struggle avoided. **Opium** or **morphine** may be

used to insure quiet under these circumstances.

**Steam inhalations** have long been employed for the purpose of increasing the secretions of mucus from the mucous membranes, softening the diphtheritic deposits, and hastening their separation. The **croup-kettle** has almost become a household utensil. To increase the efficacy of the steam, **carbolic acid**, **turpentine**, **eucalyptol**, and other aromatic antiseptics have been added to the boiling water. These measures are indicated in the cases of diphtheritic laryngitis before the antitoxin has had time to act and when the respiratory distress is not sufficiently great to warrant intubation. Here the inhalation of steam gives temporary relief. The tent should be arranged to allow ample ventilation, as otherwise the process may be very exhausting and do more harm than good. The child should not remain under the tent longer than fifteen minutes, and the treatment should not be repeated oftener than every three hours. In many cases the inhalation of steam as it comes from the kettle, without the use of a tent, is sufficient.

**LOCAL TREATMENT.**—In certain cases the local treatment in diphtheria is of importance.

The object sought in such treatment has changed considerably within recent years. We no longer seek to remove the membrane by local applications or by mechanical means, nor do we expect to destroy the bacilli in the throat. Experience has taught us that we can get rid neither of membrane nor of bacteria by local treatment, and also that too energetic efforts to accomplish these ends do harm instead of good. We have, therefore, abandoned the mechanical removal of the membrane, the application

of destructive powders or solutions to it, and the use of strong antiseptics to the affected parts. We endeavor simply to keep the nose, mouth, and throat clear of the secretions which may either obstruct them or by their decomposition and absorption increase the toxemia.

In the milder types of pharyngeal diphtheria no local treatment is necessary, the antitoxin being sufficient. In these cases, with the use of a sufficient amount of **antitoxin**, the general symptoms are very quickly relieved, the pain disappears, and the membrane is cast off. In the severer cases and in those with mixed infections, where there is great pain and when foul secretions accumulate in the mouth and pharynx, local treatment is of great value. The best method is to use the solution as an irrigation, and the best instrument for this purpose is an ordinary **douche bag**. The fluid should be non-irritating, and **normal saline**, **Seiler's fluid**, or a saturated solution of **boric acid** can be used. The patient should be in a horizontal position, lying on his side, and, if a child, wrapped in a blanket to control the arms and legs. The flow should be interrupted every few seconds to give the patient an opportunity to recover his breath. It is very important that the solution used be very hot, as the heat is of great value in relieving the pain. If the child struggles against the treatment to the point of exhaustion it should be abandoned, but, as a rule, even the smallest children become accustomed to the irrigations and rather welcome them for the relief they give. The irrigations can be given from every two to every six hours, according to the severity of the disease.

In the majority of cases of nasal diphtheria local treatment is unnecessary,

and, if not carefully given, nasal irrigations can do much harm. Certainly the incidence of otitis media is less without the use of nasal irrigations and douches. In certain of the severe cases where there is a profuse nasal discharge and great difficulty in breathing, douches are of service, but the fluid should be allowed to run into the nostrils under small pressure, always remembering the relatively large size and patency of the Eustachian tubes in infants and small children. In many instances it is sufficient to pour the fluid into the nostrils from a spoon. The solutions recommended for pharyngeal irrigations are the best to use in the nose.

Where there is much swelling of the cervical lymph-nodes, **hot or cold applications** may be used. Heat is preferable in infants; in older children the **ice-cap** may be used. **Flannel pads** or **spongiopilene wrung out of hot water**, or **poultices**, may be used in the former case.

Local treatment in diphtheria the writer believes is quite as essential as the general treatment by antitoxin. Treatment may be by irrigation, nebulization, or painting. **Boric acid** (1 per cent.), **salicylic acid** ( $\frac{1}{2}$  per cent.), **sodium chloride** (1 per cent.), etc., have been used by him, but the best results were obtained with occasional swabbing with **oxygen** solution (1 vol. perhydrol in 10 of water), followed by swabbing with a bivalent serum prepared for local use by Bandi. During the last twenty months the writer has carried out this type of local treatment in 691 cases of diphtheria; in some cases no serum was injected. The **Bahdi serum** is non-toxic, non-coagulating, and non-caustic, and causes the diphtheria bacillus to disappear more quickly than any other application. Probably the reason for its success lies in its very strong opsonic power. Appiani (Gaz. degli osped., Sept. 13, 1908).



The severe form of primary streptococcus diphtheria occurs oftener than we have been led to believe. Complications of suppuration of the cervical glands occur frequently, and complications of acute exudative nephritis occur in all severe cases and in some become chronic. In the treatment, he has found very little of any avail, except thorough toilet of the mouth and nose, with stimulation to tide the patient over the time until the toxemia subsides. Diphtheritic serum has been given even in large doses, up to 20,000 units without any effect. Antistreptococcus serum has also been given without effect. The only thing he has found of value is the spraying of the throat with **hydrogen peroxide**, **ice-bag** to the **neck**, and douching of the mouth and nose with **salt solution**. When the urine becomes scanty or suppressed, **hot rectal irrigations** or **hot-water bags** to the **region of the kidneys** are useful. Orgel (Med. Rec., Aug. 13, 1910).

Case in which, after antitoxin, throat cultures showed abundant diphtheria bacilli three weeks after start of disease. Repeated applications to the throat of a dilute culture of **Staphylococcus pyogenes aureus**, made by inoculating 8 c.c. of bouillon with a loopful of a fresh agar growth of the coccus, led to disappearance of diphtheria organisms from throat, thus preventing the child from being a "diphtheria carrier." General condition markedly improved. No untoward effects were observed. H. Page (N. Y. Med. Jour., Dec. 23, 1911).

#### GENERAL TREATMENT.—

With the advent of antitoxin most of the remedies for diphtheria have passed from use. A few still occupy a position which warrants some attention. In the treatment of pharyngeal or tonsillar diphtheria the tincture of the **chloride of iron** has long been regarded as of great value. Jacobi commends its use, advising a daily allowance of 1 dram (4 Gm.) for a child 1 year old, 2 or 3 drams (8 to 12 Gm.) for chil-

dren from 3 to 5 years old. It is to be given diluted with water and glycerin. He admits that it cannot be tolerated by some patients, and that **alcohol** is to be preferred in septic cases. Under present conditions its use must, therefore, be very limited.

In the treatment of laryngeal diphtheria the best results previous to the use of antitoxin were attained by the administration of **mercury**. The drug was given internally in the form of the bichloride, or the patient was treated by **calomel** fumigations. The **bichloride** was given in hourly doses to the amount of  $\frac{1}{6}$  to  $\frac{1}{2}$  grain (0.01 to 0.03 Gm.) in twenty-four hours, each dose being preceded and followed by copious draughts of water. This treatment was continued for from four to eight days, and good results were claimed for it.

**Calomel** fumigation was a more elaborate process. A tent or canopy was rigged over the patient's crib. Beneath this tent 15 grains (1 Gm.) of calomel were volatilized every two hours for two days and nights, then every three hours for the third day, every four hours for the fourth day, and thereafter three times a day, according to indications. The patients sometimes suffered from stomatitis and diarrhea and developed pronounced anemia; not infrequently the attendants were salivated; but this form of treatment gave better results in intubated cases than any other employed before the introduction of antitoxin.

Among other remedies that have been recommended, **pilocarpine**, **guaiaicol**, **citric acid**, **sodium hyposulphite**, and **myrrh** have received the greatest attention; but the fact must be borne in mind that, in the majority of cases treated, the diagnosis has not been

established by bacteriological examination.

**Stimulants.**—These are required in every case of diphtheria showing any marked degree of constitutional depression, most of all in septic cases. The pulse and the general condition of the patient are the guides in their administration.

The writers have employed **formic acid** in 412 patients during 1906 at the Edinburgh City Hospital, with the result of diminishing the death rate by 1.8 per cent. over that of the previous year. Previously strychnine had been given as a heart tonic, but during 1906 formic acid in 25 per cent. aqueous solution, in doses of 5 to 20 minims (0.3 to 1.25 c.c.) every four hours, was substituted, the dosage being graduated rather by the severity of the infection than by the age of the patient. No change in the heart action was noted until after about forty-eight hours, and then the change was rather a negative one, that is to say, many of the severe infections did not show the expected cardiac weakness and irregularity; on the other hand, the pulse in many instances was much improved in character, as was the color of the skin and the general nutrition. Patients were observed who appeared doomed to die of heart-failure, but who rallied, this manifestation being attributable to the possible limiting effect of the formic acid upon the degeneration of the heart muscle or its beneficial action upon the undamaged muscular tissue. The most striking result of the treatment was the diminution of the number of instances of paralysis, the percentage being only 2.9, as against 9.09 in the previous year, which was the lowest in several years. Ker and Croom (Edinburgh Med. Jour., vol. vi, p. 487, 1907).

The treatment of heart complications is prophylactic, *vis.*, **antitoxin intravenously** as soon after the onset of the diphtheria as possible. Anaphylactic shock is prevented by giving a 0.5 c.c. subcutaneous desensitizing dose 1 hour

before the intravenous therapeutic dose. Heart care should continue for several weeks following diphtheria, with gradual return to physical activities. Removal of infective tonsils and teeth will hasten complete recovery.

**Adrenalin** is probably the best drug for the cases with heart-block, as it may sustain the myocardium until a possible spontaneous resumption of normal rhythm occurs. **Strychnine**, by stimulating the suprarenals, may have a similar beneficial cardiac effect, although the suprarenals may not be able to respond. **Caffeine** often proves valuable in the later days of convalescence in improving circulatory tone, as may also **iron**, **quinine**, and **strychnine**. Digitalis is contraindicated. S. C. Smith (Jour. Amer. Med. Assoc., Sept. 3, 1921).

The writers have reported 2 cases of arrhythmia, presumably auricular flutter, in which the use of **digitalis** was followed by prompt disappearance of the arrhythmia, the tracings becoming normal except for a few extrasystoles. Both these cases had enlargement of the liver due to heart weakness. Bie and Schwensen (Jour. of Inf. Dis., Mar., 1922).

Arrest of the heart action in diphtheria is due to a paralysis of the cardiovascular system. The administration of **adrenalin** gives excellent results because of its action in increasing the blood-pressure. Munk (Jahrb. f. Kinderheilk., Apr., 1925).

A child of 3 or 4 years can take at least 1 ounce of **whisky** or **brandy** in twenty-four hours. It should be given diluted with from 4 to 6 parts of water. In the severe cases the quantity of alcohol may be increased to several times the amount named above. It is best to give it apart from the food, as the patient may decline to take the stimulant, and may be led to refuse the food because of its admixture. Next to alcohol, **strychnine** is of most value. The  $\frac{1}{100}$  part of a grain (0.00065 Gm.) may be given every two or three

hours to an infant 1 year old; twice that amount to a 3-year-old. The drug may be pushed till the deep reflexes show an exaggeration. **Digitalis** and like cardiac stimulants may be called for by the condition of the heart, but most reliance is to be put in alcohol and strychnine.

Sajous recommends **adrenalin**, 5 minims of the 1:1000 solution in a syringeful of saline solution injected intramuscularly every 2 hours.

The essentials of treatment for the heart condition accompanying diphtheria are: 1. Prompt and sufficient dosage of **antitoxin**. 2. **Rest** in bed not less than three weeks. 3. Attention to the condition of the abdominal viscera. 4. A nutritious, easily digestible **diet**. 5. Certain drugs, each according to the indications. For a slow heart, **atropine**; for a racing heart, **camphor**, and **ice** to the **precordium**; for vascular failure, **ergot**. 6. If the heart-failure is indicated to an overwhelming toxemia with lethargy, **hypodermoclysis**. Porter (Archives of Pediatrics, Aug., 1909).

**Brandy** and **strychnine**, in suitable doses, the latter administered hypodermically, are the best cardiac stimulants to administer, but they should be kept in reserve, and not exhibited too early in the disease. **Digitalis** is of more doubtful service, and must be employed with caution. Sir J. F. H. Broadbent (Practitioner, Jan., 1909).

The free use of **adrenalin** is beneficial in severe cases. One mg. ( $\frac{1}{64}$  grain) in 1:1000 solution should be injected subcutaneously every hour or two, up to 10 or even 24 mg. ( $\frac{3}{4}$  grain) daily. Kirchheim (Münch. med. Woch., Dec. 20, 1910).

The heart affection seems to be merely one manifestation of an insidious diphtheria intoxication. As the original diphtheria is subsiding after an apparently normal course, convalescence is suddenly interrupted by vomiting and the patient refuses all food, while motor agitation, even de-

lirium, alternates with apathy; there is striking pallor and the pulse is soft and faint, although the heart findings are comparatively negative. This syndrome may follow an apparently mild diarrhea, but usually the disease is of a rather severe type. The vomiting and the psychic and vascular disturbances all point to mischief in the central nervous system, the result of the action of the diphtheria toxin. Treatment must be prompt and energetic, and for this the writer commends lumbar injection of **antitoxin** and reports some favorable experiences with it, although unable to save all his patients. Bingel (Deut. Archiv f. klin. Med., Bd. civ, Nu. 3-4, 1911).

The cardiac depression must be combated by the administration of strychnine, belladonna, and adrenalin, which gave the writer four successful cases, though, of course, he has also had his failures. The formula used is as follows:—

*Atropine sul-*  
*phate* .....  $\frac{1}{400}$  gr. (0.00065 Gm.).  
*Strychnine hy-*  
*drochloride*.  $\frac{1}{400}$  gr. (0.00065 Gm.).  
*Adrenalin chlo-*  
*ride solution*  
(1 in 1000).. 5m (0.3 c.c.).  
*Water* ..... 20m (1.25 c.c.).

To be administered hypodermically every four hours. Coghlan (Brit. Med. Jour., March 9, 1912).

In a study of the toxemic stage of diphtheria dominated by cardiac (or possibly tissue) degeneration, experiments showed that a certain number of animals which otherwise would certainly have died recovered as a result of the intravenous injections of **citrated blood** in addition to **antitoxin** treatment. It is safe to conclude that in clinical diphtheria treatment along these lines will probably reduce the risk of death, and by **safeguarding the suprarenals** will shorten the illness. M. E. Harding (Lancet, Apr. 9, 1921).

The writer recalls that Morichau-Beauchant observed that diphtheria had a particularly serious effect on

the adrenals, and that Goldzicher regarded the appearance of low blood-pressure in various forms of septicemia as due to insufficiency of the adrenals. Sajous recommends the use of **supra-renal glands** of the U. S. P. by mouth for asthenia and low blood-pressure of convalescence. The powder, in 2 grain doses (0.13 Gm.), *t. i. d.*, usually suffices. With this he combines **iron** (Blaud's) and **strychnine**. H. I. Goldstein (Med. Standard, Apr., 1921).

In *post-diphtheritic asthenia* and low blood-pressure, **adrenalin**, given subcutaneously, intravenously and by rectum, is useful. It is well borne even in large doses. These cases suffer from a vicious circle involving lowered cardiac activity and impaired nutrition of the central and peripheral sympathetic system, which adrenalin overcomes. J. Munk (Ned. Maand. v. Gen., July, 1923).

The **antitoxin treatment** of diphtheria has been in general use the world over since 1895, and in that time has won for itself the right to be regarded as a specific.

The cases of diphtheria which have occurred during the past twelve years in Philadelphia, as reported to the Bureau of Health, numbered 43,997. Of this 7097 terminated fatally. With more extensive use of the diphtheria **antitoxin** the mortality has been reduced from 24 per cent. in 1898 to 12.1 per cent. in 1909. Mary Sallom (Med. Record, July 9, 1910).

Diphtheria antitoxin is taken from the blood of horses that have been subjected to repeated inoculations of increasing doses of the toxins produced by the diphtheria bacillus. The course of treatment usually occupies several months. When immunity has been thoroughly established in a horse the blood is drawn from a jugular vein into sterilized vessels and allowed to clot. The clear serum is then siphoned off into small sterilized bottles, each of which contains sufficient antitoxin for

one dose, and is preserved by the addition of camphor or carbolic acid in small quantity.

The antitoxin prepared in this manner is a clear, limpid fluid, having the color of blood-serum. If kept in a cool, dark place, it remains clear and is efficient for several months. After a year it begins to lose some of its power. Often before this time the serum becomes turbid and is unfit for use. The strength of the serum is expressed in terms of an arbitrary unit, dependent upon its power to neutralize definite quantities of diphtheria toxins. An antitoxin unit, according to the standard established by Ehrlich, is the amount of antitoxin necessary to neutralize 100 times the minimum lethal dose of diphtheria toxin for a guinea-pig of given weight. Since the reaction of different horses to the diphtheria toxin varies, the number of units in each cubic centimeter of serum will vary. Upon each bottle of antitoxin is indicated the number of antitoxin units which it contains.

The antitoxin is supposed to act in two ways. It neutralizes the toxin that has been formed by the bacilli, and also stimulates the body-cells to the production of further antitoxin. The first property is due to the antitoxic bodies proper and the latter—according to Ehrlich—to altered toxins, called by him toxons. These toxons are not toxic, and, yet, are capable of stimulating antitoxin production in the same manner as the toxin.

We have, as yet, no means of determining accurately the dose of antitoxin suitable to each case of diphtheria. It depends upon the severity of the case, the time of injection, and, to a slight extent, upon the age of the patient. We judge of the severity of the case by the location and extent of the membrane

and the degree of constitutional depression. The tendency is constantly toward the use of larger doses of the antitoxin. In the early days of its use the antitoxin was comparatively weak, and large quantities, as much as 20 c.c., were required for a single dose. Many of the unfavorable results at first reported were doubtless due to the large quantities of horse serum which it was necessary to inject. It was also a difficult and painful procedure to introduce such large quantities of fluid hypodermically.

The antitoxin now used is many times stronger; so that even the largest doses rarely require more than 10 c.c. This concentration of the serum leaves us much more free in increasing the power of the first injection.

**Dose.**—It is very difficult to formulate rules for the dosage of antitoxin, for the amount required by different cases varies greatly. One patient may require a total of 10,000 units to effect a cure, while another, with a similar type and severity of the disease, will require 40,000.

The slow absorption of the antitoxin from the tissues would seem to make the single injection by far the better method. The tables below show that the single dose gives much greater antitoxin content for the first three days.

(1) ANTITOXIN CONTENT OF BLOOD IN  
GOATS INJECTED.

(Each received 5000 units.)

METHOD OF IN- JECTION.	Units in 1 c.c. at different in- tervals of time						
	3 h.	6 h.	12 h.	24 h.	48 h.	72 h.	96 h.
Intravenous.....	4.0	3.5	3.0	2.6	2.4	2.0	1.8
Subcutaneous....	0.1	0.5	1.0	2.5	2.9	3.0	2.9
Intramuscular...	0.3	1.3	2.0	2.8	2.8	2.6	2.4

Weight of goats about 25 pounds each.

(2) ANTITOXIN CONTENT OF BLOOD IN  
THREE ADULT DIPHTHERIA  
PATIENTS.

(Each received 10,000 units)

METHOD OF IN- JECTION.	Units in 1 c. c. at different in- tervals of time.						
	3 h.	6 h.	12 h.	24 h.	48 h.	72 h.	96 h.
Intravenous (1).....	3.0	2.7	2.4	2.0	1.5	1.0	0.8
Subcutaneous (2).....	0.1	0.2	0.25	0.4	0.55	0.65	0.7
Intramuscular (3).....	0.2	0.35	0.6	0.6	0.6	0.59	0.55

Weight of number 1 about 100 pounds; of number 2 about 110 pounds; of number 3 about 120 pounds.

	UNITS IN BLOOD AT			
	12 h.	24 h.	48 h.	72 h.
Single dose.....	0.25	0.4	0.55	0.65
Dose divided into three given at 12-hour in- tervals.....	0.08	0.2	0.48	0.62

A large series of cases treated by the different methods has also shown that the **intravenous injections of antitoxin** can be safely given. In severe cases of diphtheria intravenous injections are indicated. Park (Jour. of Pharm. and Exper. Therap., March, 1912).

Having selected 125 severe cases for **intravenous antitoxin treatment** among a total of 1025 cases, the writers found that this method was of great value. The dosage ranged from 6000 to 40,000 units, the largest single injection being 24,000. In all but 11 cases the initial intravenous dose was followed by intramuscular injections, and the average total amount given was 48,000 units. The mortality rate in these severe cases was 12 per cent., and all but 32 of the 125 escaped paralyses. Toxic symptoms subsided much more rapidly. In all but 24 cases a definite reaction set in about 40 minutes after the injection. Serum sickness developed in 57. McIntyre and McKay (Lancet, June 21, 1924).

Since antitoxin is practically harmless, it can be given in large doses and

repeated as often as the condition of the patient demands. In the nasal and milder forms of pharyngeal diphtheria an initial dose of 4000 to 8000 units in children, and 5000 to 10,000 units in adults, can be given, and the dose repeated in twelve hours if necessary. If there is not marked improvement and the membrane is spreading, there should be no delay in giving repeated doses of 5000 to 10,000 units in children and 8000 to 20,000 units in adults, at six to twenty-four hours' intervals, until there is evidence that the disease is under control. The dose for children will vary with the age and size of the child, but for a child of 2 years the lower doses mentioned will not be too great, and, if necessary, can be exceeded. Usually with a granular appearance of the membrane, with loosening at its edges and relief of the constitutional symptoms in the pharyngeal type, and a relief of the stenosis in the laryngeal, there will be no further use for the serum.

The physician should, however, always be ready to give further antitoxin on indication as it is only with sufficient dosage that cure can be satisfactorily effected.

Effectual treatment consists in giving a large initial dose of antitoxin. In a severe case, from 10,000 to 20,000 units should be injected at the beginning; the result of the first injection will determine whether or no more shall be used. In severe cases of diphtheria 10,000 units by hypodermic injection are advised. If septic manifestations are evident, the most rapid relief follows the injection of 10,000 to 20,000 units into the median basilic vein. Louis Fischer (*Med. Record*, Feb. 22, 1913).

The writer deplores the timidity of certain physicians who still hold back

from high dosage and give diphtheria antitoxin in inadequate amounts. He recommends that the antitoxin be marketed in large vials, up to 20, 40 or 60 c.c., the small vials being labeled "preventive dose" and the large "curative dose." Comby (*Presse méd.*, Jan. 24, 1918).

As to the dosage of antitoxin, each case must be judged on its individual characteristics. In the writer's experience the following scale has served as a guide: 1. Purely tonsillar cases, from 5000 units to 10,000 units. 2. Laryngeal, 10,000 units to 15,000 units. 3. Pharyngeal (including tonsils), 15,000 units to 25,000 units. 4. Nasal or nasopharyngeal, 20,000 units to 50,000 units. The doses will vary somewhat according to the duration of the disease, and the possibility of more than a single type occurring in the same patient must not be overlooked. The maximum amount of antitoxin required for a given case should be administered intramuscularly into the outer side of the thigh as soon as possible. A. L. Hoynes (*Arch. of Pediat.*, Sept., 1918).

The tendency is to use a single dose of antitoxin rather than multiple doses. Subcutaneous injection requires 2 days to exert its full effect. With intravenous use the antitoxin passes out into the tissues immediately, whereas in subcutaneous or intramuscular injection it remains in the tissues and diminishes gradually for 1 to 2 weeks. Treatment, therefore, has come down to a single sufficiently large dose intravenously. In babies it is given in the jugular vein; in older children in a vein in the arm. Chills may occur after the injection, but recently an antitoxin of high potency has been prepared and filtered so as to be perfectly clear, and chills have occurred in not more than 3 per cent. The only cases in which an intravenous injection is undesirable are those in which the patients have had treatment before. Park (*N. Y. Med. Jour.*, Jan. 29, 1921).

Every hour of delay in the injection of diphtheria antitoxin may be harmful.

In mild and intermediate cases 100 units per kilo. (2.2 pounds) of body weight suffice; in severe cases 500 units per kilo. should be given. Repeated injections are unnecessary. For passive immunization, 50 units per kilo. suffice. Intravenous injection of antitoxin affords a slight improvement in the curative results, and in dangerous cases may be repeated. B. Schick (Boston Med. and Surg. Jour., Mar. 1, 1923).

To combat diphtheritic intoxication of the *medullary centers*, the writers used **antitoxin intraspinally** in doses of 20 to 40 c.c. in malignant cases, with favorable results. Large doses intramuscularly were given in addition. Benhamon, Calmette and Flogny (Paris méd., Apr. 28, 1923).

In severe cases the writer advocates further injections of **antitoxin** after 1 week, having witnessed relapse of diphtheria between the 10th and 16th days after a single injection. The Schick test was positive in these cases, and the tonsils contained no antitoxin after the 13th day, showing a lack of protection of the tissues, although the blood still contained some antitoxin. Kassowitz (Wien. klin. Woch., Mar. 20, 1924).

In the Copenhagen Blegdamshospital the mortality from diphtheria during the last 5 years was 1.2 per cent. in 4819 cases. Circulatory insufficiency (diphtheria shock) was responsible for the fatality in all but 5 of the 66 deaths; paralysis of the respiratory muscles in 4 cases, and fatal toxic action on the liver and kidneys in 1 case. The rule is **as large doses of antitoxin as possible, as early as possible**; absolute quiet; camphor subcutaneously, and **caffeine** by the mouth. Further study of diphtheria shock may disclose means to act on the capillaries, arterioles or heart musculature, and show whether adrenalin might not help. Heckscher (Ugeskrift f. Læger, Feb. 18, 1926).

In the more severe pharyngeal cases, where the physician sees the patient late in the disease, and always in laryngeal cases, an initial dose of 8000 to 15,000

units should be given to a child, and 10,000 to 20,000 units to an adult, this dose to be repeated in six to twelve hours, unless the improvement is very marked. Further treatment is to be carried out according to the reaction of the patient. When there is great improvement in the symptoms the treatment can be tentatively ceased, to be resumed on the least indication. When the improvement is slight, there should be no hesitancy in giving large doses of antitoxin at frequent intervals until there is marked improvement. In severe laryngeal cases it is well to give an initial dose of 15,000 to 20,000 units.

**Hot-air inhalations** in the treatment of diphtheria. The heated air was conveyed to the mouth by a flexible metallic tube, to the extremity of which could be attached brass tubes of varying diameter, covered by a cork cylinder in order to avoid burning the lips. The highest temperature reached by the air supplied in the apparatus was 150° C. (302° F.), but 110° C. (230° F.) was about the highest point attained in treating the patients. The method should be combined with the use of **antitoxin**, since it is complementary, the hot air being chiefly a bactericidal agency, while the serum is chiefly antitoxic. R. Rendu (Lyon méd., Jan. 12, 1913).

The writer (*vide supra*), among the 4819 patients previously referred to, had a large proportion of severe nasal and pharyngeal cases. **Antitoxin** was used in about two thirds of them in very large doses, up to 200,000 units, given partly intramuscularly in 10 per cent. of the especially grave cases. The mortality was 2 per cent.; but even of this proportion 0.8 per cent. was due to complicating diseases, pneumonia, syphilis, or lack of time for the effects of the treatment, some of the patients dying within 24 hours after admission. Of the remaining 57 deaths (1.2 per cent.) only 1 was due to a collapse after injection of the antitoxin, and the treatment may have

contributed to the fatal circulatory failure which developed in 2 other patients in the third week. Heckscher (Deut. med. Woch., Jan. 8, 1926).

The injections of antitoxin may be made in almost any part of the body, now that the quantity of serum used is comparatively small; the abdomen, thighs, or back may be preferred. An hypodermic syringe capable of holding 5 c.c. is most convenient, but the ordinary hypodermic may be used in emergency. Some slight pain, redness, and edema may be seen at the site of the injection, but nothing more, if proper care be taken in making the injection.

General eruptions may be seen in a large percentage of the cases in which antitoxin is used, if watch be kept for them. The eruption is in the form of an urticaria, as a rule, and develops about the tenth day after the injection. It may be transient and give no trouble, or may continue for several days and be very annoying.

A new method of administering antitoxin, namely, the *intraperitoneal*, is suggested for selected cases of diphtheria.

For infants and young children, the simplicity of technique over the intravenous is emphasized. Local discomfort, an annoying factor in the subcutaneous and intramuscular methods, is absent.

Absorption by the intraperitoneal route does not approach the intravenous where antitoxin is delivered directly into the blood stream. Early absorption of antitoxin, however, as shown by tests on the blood after intraperitoneal injection, is approximately 5 times greater than after intramuscular injection. Within 1 hour it is more than sufficient to neutralize the circulating toxin in the blood. Absorption by the intraperitoneal method is more rapid in infants than it is in older children. It is among the former that the procedure finds its greatest use. It is particularly applicable: (1) In advanced cases where suitable veins for

intravenous administration are lacking. (2) In moderately advanced cases in which intravenous injection is not considered necessary or advisable, but in which more rapid absorption is desired than can be obtained by the intramuscular method. Platou (Arch. of Pediatr., Sept., 1923).

After treating 50 cases with **antitoxin intraperitoneally**, the writers conclude that the method is a simple and safe one. The antitoxin is injected without dilution. They deem this the method of choice in severe cases of *toxic myocarditis*. Toomey, Goehle and Dauer (Amer. Jour. Dis. of Childr., Feb., 1925).

Temporary albuminuria has been repeatedly noted after immunizing doses of antitoxin, but this disturbance of the kidneys has always passed off without symptoms or sequelæ.

Swelling of the joints has also been reported in some cases, but must be very rare. These sequelæ of the use of antitoxin seem to be dependent upon the quantity of serum employed in the injection and the number of injections given. These disturbances, the so-called "serum sickness," are more frequent with repeated than with single injections. There seems to be a sensitizing action by the first dose, so that a subsequent one, given within a certain period, is likely to give rise to symptoms (anaphylaxis).

Park claims that the process elaborated by Gibson for refining antitoxin has reduced the incidence of rashes and "serum sickness" one-half. This process consists of the separation of the antitoxic globulins from the greater part of the non-antitoxic protein, and gives an antitoxin twice to three times as strong as the older methods.

Authorities up to the present year have failed to emphasize the occasional danger of sudden death in sensitized individuals or those subject to bronchial



asthma or to respiratory distress in other forms. Individuals peculiarly susceptible to the odor of horses or stables and those subject to asthmatic attacks, hay fever, and bronchitis should have horse serum administered only upon most urgent cause, and then with due prophylaxis. Insufficiency or inadequacy of the suprarenal glands may account in the asthmatic type for the peculiar reaction. The administration hypodermically of aqueous **extracts of the suprarenal glands** previous to the use of **serum** in this class of cases is desirable in order to rehabilitate and control the vasomotor system, and may prove of great prophylactic value, as well as useful in the heroic treatment of the acute attacks of serum sickness. Wallace (Med. Record, Jan. 7, 1911).

Warning against what the writers term the "menace of the diagnostic throat culture in diphtheria," experience having shown that lives are sometimes sacrificed through waiting for the laboratory report before antitoxin administration. The most aggravated case they refer to was that of a man who was under a physician's care for 11 days and died after the membrane had been permitted to extend to the bronchi, because frequent cultures taken in the usual way were negative. This illustrates a point sometimes overlooked: The culture *may* be wrong (even excluding laryngeal cases). The indications from this as regards early antitoxin administration in suspicious cases are obvious. Bullowa, Hardman, and Litchfield (Jour. Amer. Med. Assoc., Jan., 1923).

The effects of the antitoxin upon the diphtheritic process may be almost immediate, and should be evident within twenty-four hours in all cases. Although it has no bactericidal power whatever, it affects both the local and the general condition. In the throat an advancing process stops or at once begins its retrogression. The amount of discharge lessens, the

swelling diminishes, the membrane ceases to spread, begins to soften, and becomes looser. The favorable influence is quite as marked in the larynx as upon other parts. The stenosis is relieved, as a rule, and the membrane is more rapidly thrown off. The general testimony has been that, of the laryngeal cases, a much smaller proportion has required operative treatment for the relief of the stenosis since the introduction of antitoxin.

If **intubation** is resorted to, the tube is more often coughed out, or can be removed earlier, than under any other form of treatment.

In the asphyxia of diphtheria **morphine** will often obviate intubation, and generally the tube may be withdrawn in twelve hours. Lesage and Cl  ret (Tribune m  d., vol. xli, p. 213, 1908).

The writer intubates even infants, but he examines daily to avert pressure lesions. He had a mortality of 49 per cent. among 102 children under the age of 2 treated by **tracheotomy** when the **intubation** had failed. B  kay (Deutsch. med. Woch., Feb. 12, 1926).

The constitutional effect of the injection is as marked as the local. Usually the temperature falls within twenty-four hours, the pulse improves, the mind is clearer, and the patient is evidently better in every way.

The cases apparently severe or fatal are transformed into mild ones. Baginsky tells us that, in recording the effects of antitoxin upon the various types of diphtheria, he found it necessary to require his assistants to write their judgment of the severity of the cases upon the admission card, when each case was first seen, since the antitoxin in most cases completely changed the picture.

The time of the injection has a most

vital relation both to the immediate effect and to the ultimate outcome of the case. In experimental work an animal can usually be saved from a fatal dose of diphtheria toxin if antitoxin is given within forty-eight hours, but not later. Clinically, good results can usually be had if antitoxin is given within three days of the onset of the diphtheria, but later than that its influence is greatly lessened. In the "Antitoxin Report of the American Pediatric Society" the mortality of first-day injections was 4.7 per cent; of second day, 7.4 per cent.; of third day, 8.8 per cent.; of fourth day, 20.7 per cent., and of fifth day, 35.3 per cent.

Coupling the danger of delay with the harmless nature of the antitoxin, it is quite plain that antitoxin should be given in every case where the diagnosis of diphtheria is probable. Only in mild cases may we wait for the bacteriological diagnosis. Especially in all laryngeal cases should the immediate use of antitoxin be advised.

No harm is done if the case is not diphtheria, and, if it is, a great advantage is gained.

We may safely assume that the use of antitoxin is harmless, for if all the reported cases of sudden death, or aggravation of cardiac or renal disease, or other unfavorable influence, were accepted as proved, they could not, for a moment, be weighed against the accumulated evidence of the curative effect of antitoxin in diphtheria.

There are certain definite limitations of the efficiency of the diphtheria antitoxin. It has already been pointed out that not all the lesions of diphtheria are produced by the action of the diphtheria bacillus or its toxins.

Certain of them, especially the bronchopneumonia and nephritis, are be-

lieved to be due to the action of streptococci.

Upon these processes the antitoxin can have no direct effect. By lessening the depression produced by the diphtheria, antitoxin may enable the patient to resist the further attack of the streptococci or other pathogenic organisms; it cannot be expected to do more. It has also been urged against the antitoxin that diphtheritic paralysis is quite as frequent after its use as it was without antitoxin.

To this two reasonable replies have been made: One, that the nervous system is most susceptible to the action of the diphtheria toxins, and, therefore, most difficult to protect; so that, while antitoxin can save the life of the patient, it cannot protect him from the particular effect of this disease. The other is the ingenious suggestion that, by saving the lives of many who, suffering from severe diphtheritic infection, would, in all probability, have died under any previous form of treatment, antitoxin increases the number of those in whom we should reasonably expect to see diphtheritic paralysis develop.

The writer having lost 9 children from *diphtheritic paralysis* last year in his 622 cases of diphtheria, while 3 others died of the malignant sore throat without paralysis, he has increased the dosage in such cases and the results have been much better. In 18 unusually severe cases the impending catastrophe was warded off by the repeated **large doses of antitoxin**, while 5 others, in which the ordinary dosage was used, terminated fatally. H. Méry (Arch. de méd. des enfants, Sept., 1909).

In 6 cases of paralysis coming on 4 to 6 weeks after onset of diphtheria, the writer at once began **antitoxin**, regardless of previous treatment, and kept it up until the paralysis had disappeared. In another case it dispelled paralysis of the soft palate of 4 years'

standing. Labbé (Arch. de méd. des enf., Oct., 1921).

The method of administration of the antitoxin and its mode of action are such that it in no way interferes with the use of any other form of treatment that may be regarded beneficial. Being given hypodermically, it does not disturb the stomach or interfere with feeding or medication. Fish, of St. Louis, has reported experiments going to prove that antitoxin given by mouth is effective. Similar experiments made by Park gave negative results. It is doubtful whether any advantage would be gained if it were possible to introduce the antitoxin in this way.

As stated by Roberts (New York State Jour. of Med., Nov., 1923, cited by Therap. Gaz., June, 1924) it is now generally recognized that *if diphtheria antitoxin is used early enough, no deaths from this disease will occur*. In some instances, the physician is not called early enough. In other instances, because of poor light, or symptoms which divert his attention from the real cause of the illness, 48 hours or more go by before the true cause is recognized. In this connection an analysis of 500 deaths from diphtheria in the State of New York outside of New York City in 1922 which has been made by Roberts of the New York State Department of Health is of very great interest.

The points which deserve the chief emphasis are that in a very large proportion of the cases, namely, 369, the parents did not call the physician until the disease was well under way and in some instances interfered with proper treatment. Dr. Roberts makes a plea for educating the laity to the value of diphtheria antitoxin, and insists that the intravenous method of administration should be more widely used, especially in severe cases or in moderate cases seen later than the second day of the disease. When not used intravenously, the antitoxin should be given intramuscularly rather than subcutaneously. He believes that the subcutaneous method is so slow that it should be used only for prophylaxis in exposed

persons. When used intravenously, the patient should be desensitized by a small preliminary dose, and even if ultimately the case is proved not to be diphtheria, no harm has been done. He urges *large single doses* rather than small divided doses, stating that the full amount should be given at one time.

Proper surgical treatment should be promptly resorted to in laryngeal cases. Of 110 deaths from respiratory obstruction, 58 had no surgical treatment of any sort.

Greater attention should be paid to the care of patients during convalescence. This need is supported by the fact that cardiac involvement is stated to have played a part in nearly half of all the deaths, and that in 24 of these cardiac cases failure to keep the patient at rest was definitely mentioned as the immediate lethal factor.

Laryngeal stenosis may call for further treatment. The general testimony is that antitoxin exerts a marked, in some cases a marvelous, influence upon diphtheritic stenosis. It is also agreed that since the general use of antitoxin a greater percentage of laryngeal cases have escaped operative interference than ever before, and of those finally operated upon a greater number have recovered. The triumph of antitoxin has been that of intubation as well.

The writers highly recommend large doses of **antitoxin** and local application in the form of **antitoxin powder**, insufflated into the nose and throat until the bacilli have entirely disappeared. Perretière and Bouchet (Lyon Méd., Aug., 1918).

The results of intubation after the administration of antitoxin have been most brilliant. Whereas two-thirds of such cases died before the use of antitoxin, with it more than two-thirds recover. The indications and technique of the operation are described in the article on INTUBATION.

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**Tracheotomy** should be resorted to only when no trained intubator can

be had, or intubation has been tried and has failed. The Continental practice of resorting to a secondary tracheotomy if a tube has been worn four days rests upon no rational basis and should be abandoned. By using hard-rubber tubes, the perfection of which was one of O'Dwyer's last labors, we may leave the tubes in the larynx for months without danger of harm.

The writer advocates small, transverse incisions in **tracheotomy**. The incision should be a transverse cut upon the cricoid cartilage with elevation of a fold of the skin. On bending the head backward the wound opens so that the lower part gapes more than the upper, allowing a good inspection of the topography of this subcricoidal region. In the median line will be seen the *linea albicans*, which is to be used as a guide to cut through the muscles upon the trachea. This operation avoids severe hemorrhages, and the resulting scar is practically invisible. Leede (Münch. med. Woch., June 4, 1912).

In 2 of 4 cases observed, diphtheria was responsible for the stenosis. **Tracheotomy** was necessary in all. The tracheotomy relieved the suffocation and the heart, and allowed aspiration of the tenacious secretion, but 2 of the children died as the heart was too seriously damaged to recuperate. F. Schäfer (Archiv f. Kinderheilk., Dec. 28, 1920).

**Suction** in the treatment of *laryngeal diphtheria* has given very good results in the hands of Litchfield and Hardman (Jour. Amer. Med. Assoc., Feb. 24, 1923). The mortality was lowered from 25 per cent. in 1921 to 13 per cent. in 1922. The procedure is used promptly and as often as indicated. The patient is wrapped in a mummy bandage as for intubation and through a Jackson laryngoscope the membrane and mucus are aspirated by means of a 16 to 18 French silk or metal catheter, connected to an aspirating bottle and an ordinary electric suction pump capable of producing from 5

to 10 inches of vacuum. C. A. Thomson had already noted that a child ready for intubation was often immediately relieved by swabbing the larynx for cultures, the loose membrane often coming away with the swab and the subsequent cough clearing the mucus away, thus eliminating the need of intubation. Litchfield and Hardman found that many cases required but 1 suction treatment. In severe cases it may be repeated every 6 or 8 hours. In only 16 per cent. of suction cases was intubation later necessary because of persisting edema. Out of 158 cases of laryngeal diphtheria in 1921, 102 were intubated; out of 106 cases in 1922, only 18 (exclusive of the 9 cases of combined suction and intubation). Out of the 18 intubated cases, 8 died of terminal bronchopneumonia, while of the 46 cases treated by suction alone, only 2 died. An especial indication for suction lies in the cases with low membrane, reached neither by the intubation tube nor by tracheotomy. Suction shortens convalescence and obviates cannula troubles.

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AND

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**DISINFECTION.** See **STERILIZATION**.

**DISLOCATIONS.—DEFINITION.**—A dislocation is a permanent, abnormal, total, or partial displacement from each other of the articular portions of the bones entering into the formation of a joint.

A sprain is a temporary, partial displacement, reduced immediately and spontaneously.

In total, or complete, dislocations the articular surfaces are completely separated, or touch each other only at their edges. In ball-and-socket joints the dislocation is said to be complete when the center of the globular head is displaced beyond the rim of the concave socket.

Lesser forms of displacement are

termed partial, or incomplete, luxations, or subluxations.

A diastasis is a subluxation in which the separation occurs in a plane perpendicular to that of the articular surfaces, without lateral gliding of one upon the other. The most frequent examples of this condition are the so-called "subluxation" of the head of the radius in children and the tibiofibular diastasis in Pott's fracture.

A dislocation is complicated by injuries to surrounding tissues of sufficient importance to affect materially the symptoms, prognosis, diagnosis, or treatment. It is rendered compound if the laceration of the soft parts establishes a communication between the cavity of the joint and the outside air.

Symmetrical dislocations on both sides of the body (*viz.*, both shoulders, both hips) are termed double. If they occur in the one bone (jaw, vertebrae), they are called bilateral.

**NOMENCLATURE.**—Usually the distal member of a joint is said to be dislocated—the most notable exception is the so-called dislocation of the outer end of the clavicle (acromioclavicular joint), and the direction of the dislocation is that taken by the dislocated bone: thus a backward dislocation of the humerus means that the head of the humerus has been dislocated backward from the glenoid cavity, and lies behind it (unless it has been shifted by a secondary or consecutive displacement). Sometimes, however, we speak of a dislocation as of the joint itself, dislocation of the elbow, of the knee, here, again, the direction of the dislocation being that taken by the distal segment. Thus, instead of saying

a "backward dislocation of the humerus," we might say "a backward dislocation of the shoulder." Sub-varieties are named, according to the new anatomical position of the distal segment, as subcoracoid dislocation of the humerus, iliac (or dorsal) dislocation of the thigh.

Finally, it is well to bear in mind the distinction between "typical" and "atypical" dislocations, typical dislocations being those in which the attitude of the limb is characteristic, and atypical those in which, owing to the laceration of some opposing structure, whose integrity is usually preserved, the characteristic position is not present. An "atypical" backward dislocation of the hip is the so-called "everted dorsal," in which, owing to the rupture of the outer branch of the Y-ligament, the thigh is everted instead of assuming the usual attitude of inversion and adduction.

**ETIOLOGY.**—The factors concerned in dislocations are as follows:

(a) **Anatomic and Physiologic.**—

1. Shallow articular cups, a loose capsule, and ligaments permitting a wide range of movement, as in the shoulder and jaw, favor dislocation. Restricted movement from the interlocking of bones and from strong short ligaments reduces the tendency to dislocation. Dislocation of the bones of the shoulder is very rare, whereas fractures are common. Except in the cervical region, dislocation of the spine without fracture is uncommon. Dislocations of the hip are much less common than those of the shoulder, and of the carpus and tarsus less common than of the elbow and patella. The shoulder is more frequently dislocated than any

other joint, while 90 per cent. of all dislocations involve the upper extremity, owing to the frequency of falls upon the outstretched hand.

2. *Age*.—Intrauterine dislocations occur from failure of the joint properly to develop, from disease of the joints, ligaments, or muscles, or from trauma. Congenital dislocations are usually produced during delivery, or the child is born with conditions favoring the dislocation, which is first discovered months or years later. Dislocations from injury are rare before the age of 10, and usually occur in middle life.



Fig. 1.—Diagram to show the action of a ligament in limiting the range of motion in a dislocation. (Stimson, "Dislocations.")

3. *Sex*.—Dislocations are more common in men than in women. Certain subluxations, such as sacroiliac strain, occur more frequently in women, due to the greater ligamentous relaxation.

(b) **Traumatic**.—1. *Indirect violence*, the force being applied at a distance from the joint. This is the most common variety of dislocation by violence.

2. *Direct violence*, the force being applied directly to a joint.

3. *Muscular action*, as when the mandible is dislocated in yawning, the shoulder in pitching a ball, or the patella in kicking. Some patients can voluntarily produce subluxation, especially of the first phalanx of the thumb.

(c) **Pathologic**.—*Pathologic dislocations* are those that occur spontaneously or from slight force. They are due to diseases of the joints, such as tuberculosis, osteoarthritis, Charcot's disease, or to the wasting and weakening of muscles and ligaments in paralysis and during prolonged fevers.

**SYMPTOMS**.—Deformity is always present. The displacement of the articular surface changes the normal contour: a change which can be accurately verified by ascertaining by palpation the abnormal position of the various bony prominences; moreover, the new position of the head of the bone makes a new and abnormal center for the movements of the joint, and, in connection with the restricting influence of untorn ligaments or bony prominences, gives rise to a more or less characteristic attitude and restriction of motion in certain directions.

The comprehension of the causes which produce this constrained attitude and restricted motion, while of great assistance in diagnosis, is, in many cases, absolutely essential to intelligent manipulative treatment, for those same forces that aid our diagnosis we must take into account in our efforts to effect reduction. These forces are purely mechanical. The dislocated bone plays the part of a lever whose long arm extends from the attachment of certain ligaments to its distal extremity, and whose short arm is that part of the bone between this point of attachment and the head of the bone.

Fig. 1 illustrates how a stretched ligament causes deformity and restricted movement, and shows the danger of rough attempts to overcome the deformity. Such an ob-



stacle is not to be overcome by brute force, but rather by strategy and dexterity.

Shortening or lengthening of a limb is another aspect of the deformity. As a sign, however, it is most unreliable. Fig. 2 indicates the relative positions of the bones in a subcoracoid dislocation of the shoulder as compared with the normal joint. With the arm abducted, the shortening is marked, but in adduction there is little or no shortening; indeed, there may even be some lengthening.

Crepitation of a fibrous quality may be elicited during manipulation by friction of the bone over fibrous or cartilaginous structures, and means nothing. True bony crepitus means, of course, a fracture.

Pain is always present, and is due to two causes. There is the primary pain caused by the laceration of the tissues at the moment of the dislocation. This soon passes away. Any persistent pain is due to pressure on nerves, the stretching of untorn ligaments, an associated fracture, or other complication, and can only be relieved by the removal of the cause.

**Loss of Function.**—This is usually complete, and due partly to the pain and partly to the fixation caused by the changed relations of the bones.

**Symptoms of Old Unreduced Dislocations.**—Deformity of contour and attitude, as well as restriction of motion, will persist as long as the dislocation remains unreduced; but, as the parts tend to adapt themselves to their altered conditions, a new socket may form and the disability becomes progressively less until the functions of the limb can in part be fairly well performed. But sev-

eral conditions may interfere with this restoration of function. An excessive production of cicatricial tissue may limit or abolish the motions of the joint; the head of the bone may be progressively displaced farther from its normal situation, and the disability thus become greater instead of less, or an intractable neuralgia or edema may result from pressure on adjoining nerves or vessels.

**DIAGNOSIS.**—There are six important indications of dislocation: 1. Preternatural immobility or ab-

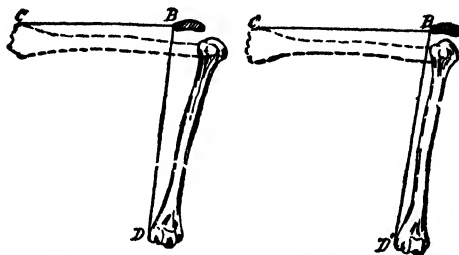


Fig. 2.—Diagram to show the effect of attitude upon the measured length of the arm (1) in dislocation of the right shoulder, and (2) when the bones are in a normal position; *B, B*, the acromion, ("American Text-book of Surgery.")

normal restriction of movement, which may be contrasted with the abnormal point of movement or preternatural mobility found in fractures. 2. Abnormal relation of the bony prominences of a joint. 3. Abnormal relation of the articular surface as shown by position of the limb, palpation, or X-ray. 4. Changes elicited by mensuration. Shortening or lengthening of the limb, which may vary with the position, or alteration in the various circumferences or diameters of the joint, apart from that produced by local swelling. 5. Deformity, including the change in contour of the joint, and the peculiar position in which the

limb is held. 6. Reduced function. The dislocated lower jaw cannot be closed. With a dislocated shoulder, the elbow and wrist cannot be simultaneously apposed to the chest.

The most demonstrative sign of dislocation is the recognized presence of the head of the dislocated bone in an abnormal position. One may make the same inference from the negative evidence; namely, the absence of the head of the bone from its normal situation.

In such localities as the fingers or knee the head of the bone may be seen; elsewhere it may be felt, as in the jaw (forward) or the shoulder, or, again, the diagnosis may only be ascertained by finding an indefinite mass which partakes of the motions imparted to the bone. Measurements may help; but, as above noted, are liable to mislead.

In typical dislocations the attitude of the limb and the limitation of motion are usually the first hint the surgeon obtains of the nature of the case; but, we repeat, the only conclusive evidence is the discovery of the head of the bone out of its normal place.

**Differential Diagnosis.**—The differentiation of a simple dislocation from a fracture at or near the articular surfaces is often difficult, sometimes impossible without an X-ray study. If the fracture is through the neck of the bone (without impaction) the dislocated head will not move with motions imparted to the shaft of the bone; but will, on the contrary, give rise to a bony crepitus, unless some soft parts are interposed. But if the fracture consists simply of the splintering of an articular edge, or the tearing off of a tuberosity, the

fragment may be pushed or drawn away and give no evidence, except perhaps a weakness in the joint, a lack of certain motions, or a tendency to recurrence of the dislocation, for which we can only assign the fracture as a probable cause.

In fractures mobility is created where before it was not. In dislocations it is decreased in some directions, but it is not infrequently increased in others, and, indeed, with sufficient laceration of all the soft parts it may be increased in all directions. In case of doubt a dislocation may be differentiated from a contusion or sprain by examination under ether or by the X-ray.

**PATHOLOGY OF RECENT DISLOCATIONS.**—In joints relaxed by paralysis or effusion (and in the jaw) dislocation habitually takes place without laceration of the capsule. In all other cases (excepting the voluntary dislocations before mentioned) the capsule is torn. In enarthrodial joints the rent is on the side toward which the round head of the distal bone is displaced. In other joints any or all of the ligaments may be torn. The firmer bands, instead of giving way themselves, may strip up the periosteum or tear away the bony prominences to which they are attached. Opposing muscles put upon the stretch may act in the same way. The bones may also be broken by impact on each other; thus fracture of the olecranon occurs in anterior dislocation of the elbow, and a mutual bruising of the head of the humerus and shattering of the rim of the glenoid cavity in dislocations of the shoulder.

**COMPLICATIONS.**—Fractures worthy of the name of complications

may occur. Some, indeed, such as fracture of the anatomical neck of the humerus, may prove insurmountable obstacles to reduction. External wounds, especially if they compound the dislocation, may prove serious complications. Adjoining vessels may be ruptured and give rise to fatal hemorrhage, or to occlusion and gangrene, or to traumatic aneurisms. The rupture of nerves may cause permanent paralysis and anesthesia. The viscera are rarely injured unless by some other associated trauma.

In old unreduced dislocations the lacerated connective tissue about the head of the bone becomes thickened and forms a pseudocapsule, while the periosteum, on which the head of the bone now rests, is stimulated and throws out a ridge of bone so as to form a new articular cavity, sometimes lined with fibrocartilage. The muscles and ligaments shrink or elongate to adapt themselves to their changed circumstances, and thus a comparatively useful new joint may be formed. In the meanwhile an opposite train of events takes place in the old joint cavity. It is obliterated either by adhesion of the capsule or by filling up with granulation tissue. Thus not only is the dislocated bone fixed in its new position, but also the old socket is obliterated and rendered unfit for its reception. It is important to note that the scar may include neighboring vessels or nerves, and by pressing on them give rise to neuralgia or edema without any direct pressure by the bone itself, and, moreover, the tearing of this tissue in attempts at reduction may result in fatal injuries to vessel or nerve.

**PROGNOSIS.**—Reduction is usually followed by repair of the dam-

age done, and within a few weeks the joint is as useful as ever. Occasionally, however, a permanent laxity of the capsule remains, which allows the dislocation to recur on more or less slight provocation, and with each recurrence the tendency grows more marked. Occasionally, also, without any unusual evidence of injury to the nerves at the time of occurrence of the accident, a dislocation may be the starting point of an intractable neuralgia, or it may predispose the joint to rheumatism. The complications above mentioned render the prognosis more grave.

In old unreduced dislocations the prognosis is different for every individual case. In some the new joint will become fairly useful, in others not so; yet the prospect of relief by operation is not always good.

**TREATMENT.**—A recent dislocation should be immediately reduced unless great inflammatory reaction, swelling, or shock renders the infliction of pain or the use of anesthetics inadvisable.

Anesthetics are of use to overcome the resistance of the muscles, which, contracted by pain or fear of pain, oppose the manipulations necessary for reduction, or in case the patient can not or will not suffer the pain incident to those manipulations. Reduction may usually be effected in "primary" anesthesia. Ether is safer than chloroform for this purpose. Nitrous oxide is less useful than the more relaxing general anesthetics. Spinal anesthesia gives excellent relaxation for dislocations below the level of the diaphragm. Local anesthesia produced by the distention of the capsule with a  $\frac{1}{2}$  to 1 per cent. procaine solution will at times abol-

ish reflex spasm and permit of a nearly painless reduction. The older surgeons produced relaxation by emetics, such as tartar emetic, iobelia, or enemas of tobacco.

The choice of the method of reduction depends upon the recognition of the obstacles to reduction. Aside from muscular opposition, the usual obstacle is the resistance offered by untorn ligaments or portions of the capsule to movement in certain directions. Other obstacles are interposition of the ligaments or muscles, and these may be of such a nature as to demand operative interference.

The older methods of reduction by means of direct pressure on the head of the bone or traction by hand, by pulleys, or by electric force, have been, in great measure, superseded by the more scientific and practical method of reduction by manipulation, in which, by a succession of gentle movements, the head of the bone is brought opposite the tear in the capsule, the opening is enlarged by relaxation of its sides, and the head of the bone slipped into place by leverage on the untorn portions of the capsule and ligaments, aided, if need be, by traction and pressure on the bone.

In old dislocations the manipulations useful in recent cases are much less likely to succeed, owing to the firm adhesions binding the head of the bone in its new situation and the obliteration of the disused articular cavity. Moreover, strong traction may be required to overcome the contraction of the muscles. Interference in such cases is unavoidably blind and uncertain, and involves much more extensive laceration than took place at the time of the original

injury. So many accidents have followed attempted reduction by manipulation in these cases that, if cautious manipulation fails to effect reduction, it is better to leave the dislocation unreduced in the majority of cases, or, if the loss of function is so great as to induce the surgeon to run the risk, an open arthrotomy may be done with the hope of dividing the opposing structures, opening up the old socket, and replacing the dislocated bone.

The accidents which follow ill-advised attempts at reduction are usually fracture of the bone or rupture of vessels, leading to hemorrhage, gangrene, or aneurism. More rarely injury to large nerves has occurred, and even complete avulsion of a limb has been recorded.

In old dislocations, with contraction, prolonged preliminary traction may be used to gradually stretch the shortened tissue and to permit reduction with the least danger to the vessels and nerves.

**After-treatment.**—After reduction the joint need usually be kept immobilized only a few days, and excessive motions avoided for a few weeks. Some dislocations require special dressings (*e.g.*, clavicle). Gentle passive motion should usually be begun within at least three weeks to prevent adhesions.

Habitual dislocations have been cured at the inner end of the clavicle by periarticular injections of alcohol (Stimson) and at the shoulder by injections of tincture of iodine. But this method of producing adhesions offers so grave risks of ankylosing the joint that in the more important joints it is advisable, if the tendency cannot be overcome by the prolonged

wearing of an immobilizing apparatus, or one which allows only slight motion, to excise, or take a "reef" in, the lax portion of the capsule, and to suture or reinforce stretched or torn ligaments.

In the event of purulent infection, *Willem's treatment* by active movement is of great value. Free drainage is obtained, but no foreign body introduced into the synovial sac. Weight and pulley extension is applied and the patient passively and actively made to move the joint freely every two hours. The movement, at first painful, soon becomes practically painless. The pus is forced from the synovial cavity by the movements, and the patient recovers with a movable joint. Very free use of the joint is insisted upon after the third week.

**Positions to be Maintained When Ankylosis is Feared.**—Much disability may be saved by keeping joints that may become ankylosed in the position of greatest usefulness. We are indebted to Robert Jones for studies of this subject.

In the case of the shoulder joint, the arm should be treated in an abducted position of about  $50^{\circ}$ , with the elbow slightly in front of the plane of the body.

At the elbow joint, an angle of about  $70^{\circ}$  is the most useful position, unless both elbows are involved, when one should be fixed at an angle of about  $110^{\circ}$  and the other at  $70^{\circ}$ .

In the forearm, the preferred position is usually a neutral position between pronation and supination. For certain laborers, however, complete supination is desirable.

At the wrist joint, all injuries

should be treated in a position of dorsiflexion, which improves the grasp of the fingers.

At the hip joint, ankylosis should be permitted only in very slight abduction, with the thigh extended and slightly rotated outward.

At the knee, the joint should be fixed in an extended position or at an angle of  $70^{\circ}$ .

At the ankle, the foot should be kept at right angles with the leg and in a slightly varus position. The normal arches of the foot should be supported, and slight inversion should be maintained.

**CONGENITAL DISLOCATIONS.**—Under this head are included all dislocations supposed to have existed at birth—although sometimes not diagnosticated for months or years.

Congenital dislocations of the hip cover about 90 per cent. of all cases. They are more frequent in females than in males. One or both joints may be involved. The typical cases are caused by a defective development of the Y-cartilage and acetabulum, which permits the influence of the weight of the body, or the contraction of the muscles, to drag the head of the bone out of the socket on to the dorsum of the ilium.

It is of great importance that congenital dislocation of the hips be diagnosed early, as the best results can be obtained only in cases which are seen in the first 7 or 8 years of life. With the aid of Röntgen plates the diagnosis should not be difficult. The difficulty of reduction increases as the child's age advances. It is generally hard to reduce bilateral cases after the age of 6 and unilateral cases after 8 years, and reduction should not be attempted when the shortening exceeds 2 inches.

The writer agrees with Ridlon that in the majority of cases the dislocation is superior and not posterior. In the superior dislocations the head can be felt in front on outward rotation of the limb and at the back on inward rotation; in the anterior type the head is felt in front but not in back on inward rotation; while in the posterior type the head can be felt at the back and not in front on outward rotation. Ridlon states that few of the anterior dislocations remain in when replaced, while about 75 per cent. of the superior dislocations remain secure when replaced. In bilateral dislocations perfect results in both hips are obtained in about half of the cases. The chief difficulty in obtaining a successful reduction is the shallow acetabulum. Packard (*Colo. Med.*, xv, 138, 1918).

After careful anatomical studies the writer found that the conditions in the fetal hip joint as term approaches greatly favor dislocation, the cramped position tending to force out the femoral head. At birth, great care should be taken to allow the child's legs to straighten out spontaneously; forcible straightening at this time stretches the attachments and induces the clinical picture of dislocation. Harrenstein (*Ned. Tijds. v. Gen.*, Nov. 8, 1924).

Pubic and obturator dislocations are very rare. As the child begins to walk the head is pushed farther upward until it is finally arrested and a new joint formed. The head of the bone is small and deformed and the real acetabulum largely obliterated. Compensatory changes appear in the pelvis, which is tilted forward, and the lumbar spine, which is curved forward. If one hip alone is involved, there is an additional lateral curvature, and the child limps; if both are involved, there is no limp, but the gait is peculiar. The tilting of the pelvis can be made to disappear

by placing the child upon its back and flexing the thighs.

The prognosis as to the utility of the limb is fair. The patient will probably be able to get about, and the deformity will grow no worse.

Report of a commission on congenital dislocation of the hip appointed by the American Orthopedic Association. In 201 of 713 cases the right hip was involved; in 288, the left; and in 224, both hips. In 348, reduction had been effected by the Ridlon method, in 150 by the Lorenz method, in 80 with the Bradford machine, in 80 with the Hibbs table, and in 12 by open operation. The Lorenz position was used after reduction in 188 cases, and the Lange position in 140. In some clinics the first cast remained in place for 4 months; in others it was changed at 1 month. Some clinics permitted walking early; others, not until the cast was left off.

Among 156 patients over 6 years old, 54 were found to be in after 3 years; 60, out; 13 marginal or anterior; and 6 questionable. Among 414 cases under 6 years old, in which 521 hips were treated, 320 were in, 93 out; 51 marginal or anterior, and 2 questionable. The ratio of successful results in patients over 6 years of age thus appears to be 26.8 per cent. while for those under 6 it is 60.1 per cent. Goldthwait and Adams (*Jour. Orthop. Surg.*, iii, 353, 1921).

**TREATMENT.**—Palliative measures should be resorted to in those cases which have reached adult life unrecognized or untreated. For this purpose an elevated sole to the shoe, or a corset stiffened by steel with a pad to limit the upward displacement of the trochanter may be used.

Reduction by forcible manipulation, as perfected by Lorenz, is especially applicable in children from 2 to 7 years of age. Under anesthesia the leg is forcibly rotated outward

and inward, then abducted so that the thigh lies at right angles to the trunk in the flexed position. During this process the adductor muscles are forcibly massaged. Forcible flexion until the thigh touches the abdomen is carried out. The child is then placed on its face and the leg hyperextended and abducted. The force of these manipulatory movements must be sufficient to relax the muscles completely. The reduction is accomplished by abduction, rotation, and flexion, as in the traumatic cases, and in favorable cases the head slips into the acetabular cavity with a click. After reduction a plaster spica bandage is applied with the limb in a position of right-angled flexion and abduction. After two weeks the cast may be cut away below the knee and the child allowed to walk. This bandage is removed in two or three months and the leg put in a less degree of flexion and abduction for three months longer. Fixation should be continued until the joint stability is assured, and usually consumes a period of from six months to a year. After the removal of the cast massage, active and passive movements, should be thoroughly carried out.

The bloodless replacement usually called the "Lorenz operation" was used by the writer only to discard it.

The writer's method is as follows: The patient's flexed knee is grasped and the thigh fully flexed on the body. The operator finds the greater trochanter, neck and head of the femur with the fingers of his other hand and places the thumb of that hand in front below the antero-superior spine of the ilium. The femoral head is then pushed downward to a position opposite the lower part of the rim of the socket. The

thigh is abducted, while the opposite side of the pelvis is held firmly down by an assistant, and the head can be felt by the operator's fingers and thumb passing forward and into the socket.

When the limb has been placed in the most secure right-angled abduction position, the stockinette and sheet wadding are applied. With the patient's body resting on a sacral and back rest, plaster bandages are applied to make the permanent plaster cast. It is necessary to extend the plaster down on the leg with the knee bent at right angles to prevent the thigh from rotating. Frequently but 1 cast is applied, which remains for 8 months. In older cases the first cast is removed at the end of 4 months, and after the legs are brought nearer together a new cast is put on; sometimes a third is applied.

When the cast has finally been removed, the mother or nurse makes a gentle inward rotation and stretching downward of the legs until, after daily efforts, the limbs are brought together and the toes point directly forward. *J. Ridlon (Surg. Clin., i, 271, 1917).*

The writer modifies the Lorenz technique by substituting for the violent manipulations gradual extension:

- (1) Application of extension in the lines of the legs as they rest in their deformed position.
- (2) Gradual abduction until the legs form with each other an angle of 180 degrees.
- (3) When the maximum abduction has been produced, digital manipulation of the heads of the femurs to drop them into place.
- (4) Maintenance throughout of the degree of rotation necessary to keep the toes pointing directly upward.
- (5) Gradual reduction of the maximum abduction produced until the legs form with each other an angle of about 35 degrees.
- (6) Application of a plaster cast from the waist to the knees.
- (7) Transmission of the body weight to the acetabula through the heads of the femurs by allowing the child to walk. *J. W. Churchman (Surg., Gynec. and Obstet., xxviii, 518, 1919).*

The neck of the femur should be kept in a horizontal rather than a slanting position throughout treatment. In the first cast the thigh should be flexed to  $1\frac{1}{2}$  right angles, in the second to 1, and in the third to  $\frac{1}{2}$ . Calot (*Bull. de l'Acad. de méd.*, Apr. 20, 1920).

The writer uses a special lever-tractor to pull the head of the femur down into place. He also hollows out the acetabulum deeper and carves the femoral head to correspond. He finds the operation easier in adults, and recurrences less frequent. Lambotte (*Arch. franco-belges de chir.*, Dec., 1921).

Reduction should usually be manipulative. If it fails, the limb should be put in **plaster** in flexion, abduction, and outward rotation for 1 or 2 weeks, and another trial at reduction then made. If this also fails, another cast should be supplied and removed in 2 weeks, the skin prepared for 4 days, and **the hip opened** for reduction. Direct reduction without preparatory stretching is indicated if the patient is between 3 and  $4\frac{1}{2}$  years old and shortening does not exceed  $1\frac{1}{2}$  inches. If the muscles give resistance, repeated stretching is necessary. In most cases fixation should be continuous for 7 to 10 months. II. B. Thomas (*Jour. Amer. Med. Assoc.*, Feb. 4, 1922).

The writer generally uses the **Lorenz method**, though without following it strictly. The leg is retained in a spica at right angles for at least 6 months, and in older patients it is re-applied once or oftener with diminished abduction. **Massage, exercise and passive stretching** are carried out later for several months. If treatment is given by the third year of life, anatomical reduction should be obtained in 75 per cent. of unilateral and 50 per cent. of bilateral cases. Imperfect results should be followed by open operation to make a lip for the acetabulum without opening the joint. Fairbank (*Brit. Jour. of Surg.*, July, 1922).

For older cases or cases in which the above does not succeed, the open operation is indicated.

Of the operations, that of Lorenz is a type. He makes a vertical antero-external skin incision, divides the fascia lata transversely, separates the muscles, frees the bone by a cross-cut in the anterior surface of the capsule, gouges out the old acetabulum, making a strong upper rim to it, and replaces the bone by extension, aided by a traction apparatus. Immobilization is replaced by passive motion at the end of four weeks, and the child begins to walk with assistance two weeks later. No further apparatus is used. In difficult cases Lorenz advises a preliminary course of two weeks' extension by a thirty-pound weight.

The writer has devised a new operative technique—the **bifurcation method**—for irreducible luxation of the hip, congenital or acquired. By a slanting osteotomy of the femur, a new head is carved out on a level with the acetabulum, into which the new head is fitted. The upper end of the femur thus assumes a Y shape, and the leg is slightly shortened. The operation can be carried out without exposing the joint, and is feasible at any age.

In the simpler cases of luxation, he prefers the **inversion method**, in which the adductors are stretched or severed, thus transforming the usual adduction into extreme abduction, drawing the ilium downward, affording bony support to the greater trochanter, and throwing the weight of the body partly on the strong anterior portion of the ligamentary apparatus. Lorenz (*Nederl. Tijd. v. Gen.*, May 26, 1923).

The anterior knee dislocations are easily reduced, and a good functional result may be predicted.

### SPECIAL DISLOCATIONS.

#### Dislocations of the Lower Jaw.—

The dislocations may be single or double. Upward or backward dislocations are very rare. In the former the condyle is driven through the base



of the skull; in the latter, back through the anterior wall of the external auditory meatus.

*Forward Dislocations.*—The lower jaw projects forward, the mouth cannot be closed, the condyles may be seen and felt in front of the eminentia articularis. The glenoid fossa is empty. In unilateral dislocations the chin is deviated to the opposite side. The pain is usually not great.

The usual cause of forward dislocations is a wide opening of the mouth in yawning, laughing, or introducing some large object. It is more frequent in women than in men. When the mouth is wide open the external lateral ligament is relaxed and the external pterygoid muscle draws the condyle, and the interarticular cartilage with it, well forward on the eminentia articularis. A slight overaction of this muscle carries the condyle over the summit, and is then held by the balance of forces between the muscles pulling upward and forward and the external lateral ligament pulling upward and backward. The interarticular cartilage accompanies the condyle, at least part of the way. The capsule is not torn.

Reduction is accomplished by opening the mouth more widely to relax the ligament and then pressing the condyle backward and then a little downward. A fairly successful method is by grasping the jaw on either side with the padded thumbs on the molar teeth and the fingers under the jaw outside. As the jaw snaps back the thumbs must be quickly slipped into the hollow of the cheeks to avoid being bitten. Reduction of one side at a time is sometimes easier. A square, notched stick of wood, placed well back between the molars and rotated as the chin is pushed up and

back, avoids injury to the operator's thumbs. Anesthesia may be required to overcome the contraction of the muscles.

Not infrequently this dislocation tends to become habitual. To overcome this the meniscus may be sutured in place, or, which is easier, the hypodermic injection of 1 or 2 c.c. of 80 per cent. alcohol or of 10 to 20 minims of tincture of iodine given a trial.

Recurrent dislocation of the jaw occurs infrequently. It is a painful and disabling condition and tends to grow worse. The coronoid process or the insertion of the temporal muscle into it should be tied up to the anterior part of the zygomatic arch, with silver wire or with slowly absorbable suture material. The operation is less difficult than attack on the temporomaxillary joint, does not injure important structures, and the scar is not disfiguring. The result should be 100 per cent. success. J. B. Blake (*Trans. Amer. Surg. Assoc.*, June, 1918).

Report of a case of recurrent unilateral subluxation of the jaw in a girl of 16 years, in which the X-rays showed that the mandible rode forward on the maxilla. At operation the masseter muscle was detached subperiosteally and a small triangular flap of skin and muscle turned down. The cartilage, loosely attached, was caught in a tenaculum and removed from the condyle with scissors. The patient had no further trouble. A. P. C. Ashhurst (*Annals of Surg.*, lxxiii, 712, 1921).

**Dislocations of the Spine.**—Except in the cervical region, dislocations of the spine are usually associated with fracture (fracture dislocations). (See FRACTURES, in this volume).

**Dislocations of the occiput** from the atlas and of the atlas from the axis may be unilateral or bilateral. In

unilateral dislocations, there is lateral deviation of the chin, and in all cases movements of the head and neck are restricted and painful and the head is usually held in an abnormal position.

[Of three cases of unilateral dislocation of the atlas without cord symptoms, observed personally in soldiers, two followed falls upon the head, and one the manipulation of the head incident to tonsillectomy under local anesthesia. W. WAYNE BABCOCK].

The diagnosis is made by the painful fixation and position of the head and neck, the deviation of the cervical spines, alterations in the relation of the cervical bodies felt through the mouth, and in particular, carefully made roentgenograms. Dislocation of the odontoid process from behind its ligament, which the hangman aims to produce in legal execution, is instantly fatal from pressure on the medulla.

The treatment should consist of early attempts at reduction, with roentgenograms as a guide, by cautious extension, angulation to unlock the vertebra upon one side, and rotation. With fracture of the odontoid process, manipulation may be very dangerous. Operative reduction may be very difficult and in certain cases may properly be limited to the removal of sufficient bone to relieve pressure.

Laceration of the medulla, with or without fracture of the odontoid process, causes instant death in most cases.

Two cases in soldiers who showed immediate quadriplegia, the one after dislocation of the atlas and axis with fracture of the odontoid process, the other following backward luxation of the fourth cervical vertebra. The second case developed sphincter dis-

turbances. After a period of spinal coma, lasting 6 weeks in the first patient and 4 months in the second, the quadriplegia underwent retrogression in a crossed manner, return of motion taking place simultaneously in the upper extremity of one side and the lower extremity of the other. Ten months after the injury motor recuperation was almost complete in both cases, the first patient still showing traces of left sided hemiplegia and distinct hyperesthesia in the great occipital distribution, the second a right sided brachial monoplegia and hyperesthesia of the third cervical. Roussy and Cornil (*Presse méd.*, May 13, 1918).

Stress laid on partial deviations of the cervical vertebrae, due usually to direct injuries of the head or neck, or to falls. Incomplete luxations of the cervical vertebrae are much more frequent than is believed. Pain, stiffness, and inability to move the head are frequent symptoms. As a rule the displacement may be reduced almost or quite painlessly by appropriate movements. C. F. Cyriax (*Jour. de Chir.*, xv, 457, 1919).

In a case of fracture dislocation of the third cervical vertebra treated by the writer, **head traction** with a 6-pound weight was applied night and day for 3 days, and judicious **manipulation** in the proper direction then made. The patient had a remarkably good return of function, having only slight limitation in rotation and lateral bending of the head. Goddu (*Boston Med. and Surg. Jour.*, Feb. 17, 1921).

**Dislocation of the Lower Cervical Vertebrae.**—This may be double or single, complete or incomplete, forward or backward, or bilateral in opposite directions. If the dislocation is unilateral (forward), the head is turned to the opposite side, on which side the muscles are contracted. On the side of the dislocation the dislocated bone may be felt, and its spinous process is deflected toward that

side. In bilateral forward dislocations the head may be bent far forward and the dislocated bone (usually the fifth) felt in the back of the neck, or the head may be extended and the bone palpable within the pharynx. The symptoms depend upon the amount of injury to the cord. Damage to the cord above the third cervical vertebra causes death by cutting off the phrenic nerves. Below this point the result will be a paralysis more or less durable according to the nature of the lesion.

The mechanism of the unilateral forward and bilateral dislocations in opposite directions is abduction (lateral flexion) and rotation, by which the inferior articular process of the upper vertebra is lifted over the superior process of the lower one. Bilateral forward dislocations are caused by hyperflexion; backward, by hyperextension and direct pressure.

*Treatment.*—Reduction should be attempted at once. Unilateral dislocations are to be reduced in the way they were produced, *i.e.*, by increased abduction and traction (to free the edge of the process), followed by adduction and rotation, aided by direct manipulation, so as to lift the disarticulated bone back into place.

Traction and local pressure have proved effectual in the reduction of bilateral dislocations.

After the reduction the patient should be kept quiet for some weeks. A plaster-of-Paris splint for head and neck is advisable.

Two cases of dislocation of cervical vertebræ reduced manually without anesthesia. One case was a dislocation of the fifth cervical, rotatory in type, the left side having moved forward, the right side slightly backward. Placing the patient in a sitting

position in bed, grasping the head beneath the occiput and chin, the writer was enabled, by forcible extension which nearly lifted the patient's whole body weight, to make rotation and correct the deformity. A very slight jar was perceptible when the head was released; it returned to its former deformed position, without any snapping sound or subjective sensation, and without increased pain. A month afterward a plaster-of-Paris encasement was applied to hold the head in a slightly overcorrected position with some extension. Speed (*Annals of Surg.*, Dec., 1917).

These means failing, if there seems any hope of recovery by removing the pressure from the cord, the dislocation should be cut down upon aseptically and an attempt made to reduce it by removing such ligamentous or bony obstacles as may exist.

**Dislocations of the Sternum.**—Dislocations, forward or backward, of the body from the manubrium are usually accompanied by serious interference with respiration and circulation. From fracture the diagnosis is made by finding the second costal cartilages attached to the manubrium and torn from their articulation with the body. Inasmuch as the injury is due to great violence, direct or indirect, the associated injuries play a large part in the prognosis. Reduction is effected by dorsal flexion and direct pressure.

**Dislocations of the ensiform process** are a tilting either forward or backward. The symptoms are pain and persistent vomiting. Pressure with fingers or a sharp hook passed beneath the skin will yield reduction, or the process may be excised.

**Dislocations of the Ribs and Costal Cartilages.**—The ribs may be dislocated forward from the spine or forward or backward from each other or from their costal cartilages. The

cartilages may be dislocated from the sternum.

The symptoms and treatment are the same as of fracture of the ribs: Reduction, followed by the application of a tight band of adhesive plaster three-fourths of the distance around the chest. Chondrosterneal dislocations usually recur.

**Dislocations of the Inner End of the Clavicle.**—The clavicle may be



Fig. 3.—Adhesive-plaster dressing for upward dislocation of acromial end of clavicle. (*"American Text-book of Surgery,"*)

dislocated forward, backward, or upward, in this order of frequency.

Forward dislocation may be complete or incomplete. The head of the bone is prominent and may be displaced inward. The shoulder sinks downward and inward. The arm is useless. There is local pain. This dislocation is usually caused by a forcible depression and pushing backward of the shoulder, by which the center of the clavicle comes to rest on the first rib, and on it as a fulcrum the inner end is pried upward

and forward. By pulling the shoulder upward and backward and pressing on the dislocated bone reduction is effected; but retention is often difficult. Dorsal decubitus with the shoulder pressed forward may prove effective or may be reinforced by direct pressure by a molded plaster-of-Paris splint, a hernial truss, or a pad retained in position by adhesive plaster, or a figure-of-8 bandage, crossing in front. If all precautions fail and the dislocation becomes habitual, 2 or 3 biweekly alcohol injections with immobilization may be tried, the capsule exposed and shortened, or ligation or wiring used.

Backward dislocations may be either complete or incomplete. The head of the bone passes backward and may compress any of the important structures at the root of the neck. This dislocation may be caused by direct violence or by forcing the shoulder forward and inward. Reduction is effected and maintained by drawing the shoulder backward and outward and retaining it in that position.

Upward dislocation is caused by depression of the shoulder. The head of the bone rests on the episternal notch, having passed behind the sternal head of the sternomastoid. Reduction is made by drawing the shoulder upward and outward and pressing the head of the bone down. Here, again, retention is difficult, and wiring or suturing are procedures which may be considered.

**Dislocations of the Outer End of the Clavicle.**—The usual variety is upward or upward and outward. Rarely a subacromial dislocation occurs. The so-called subcoracoid dislocations are probably mythical.

**Upward Dislocation.**—The acromial end of the clavicle rises more or less above the acromion, and may be displaced outward over it. There is frequently fracture of the articular edges. The usual cause is a blow on the shoulder. Reduction is easy; retention, difficult. Non-reduction causes almost no loss of function and but little deformity. Stimson's retention dressing is recommended for its simplicity and efficiency (Fig. 3). A long strip of adhesive plaster three inches in width is placed with its center under the point of the flexed elbow and its ends carried up in front of and behind the arm, crossing over the end of the clavicle, and secured to the front and back of the chest, respectively, while the bone is held in place by pressure upon the clavicle and elbow.

Recurrence can be readily detected through the plaster. For additional security the forearm should be supported in a sling, and the arm bound to the chest.

**Subacromial Dislocations.**—A few cases are recorded in which the outer end of the clavicle was forced down and caught under the acromion. Direct violence and muscular action are the recorded causes. Reduction was easy by drawing the shoulder outward, and there was tendency to recurrence in only one case.

**Dislocations of the Shoulder.**—These dislocations are as numerous as all other dislocations taken together. They are rare in youth and old age, and more frequent in men than in women. This frequency is explicable by the exposure of the joint to trauma and its conformation. The glenoid cavity covers such a small part of the head of the humerus that, in extreme degrees of abduction, extension, or flexion, any force

transmitted through the shaft of the bone is applied obliquely in the bony surface and directly on the capsule of the joint, through which the head of the bone is then forced.

**Varieties.**—Four divisions may be made according to the direction in which the head of the bone leaves the socket, and these subdivided according to the point at which it comes to rest, or according to the position of the limb, as follows:—

- |               |   |                              |
|---------------|---|------------------------------|
| Anterior ...  | { | Subcoracoid (most common).   |
|               |   | Intracoracoid (exceptional). |
|               |   | Subclavicular.               |
| Downward..    | { | Subglenoid (uncommon).       |
|               |   | Erecta (very rare).          |
|               |   | Subtricipital.               |
| Posterior ... | { | Subacromial (rare).          |
|               |   | Subspinous (very rare).      |
| Upward .....  |   | Supraglenoid (very rare).    |

In the anterior dislocations the displacement is also more or less downward (and, of course, inward), and in the downward ones it is usually also forward and inward. Thus, the two classes merge into each other. The term "subglenoid" is restricted to those cases in which the head of the bone is very low, others of this class being called "subcoracoid." The accompanying figure (Fig. 4) will demonstrate the different positions assumed by the head of the bone in the anterior-and-downward dislocation.

**Anterior Dislocations.**—The subdivisions of this variety are dependent on the increasing amount of inward displacement of the head of the bone, and grow less frequent in the same order; namely, subcoracoid, intracoracoid, and subclavicular.

**Subcoracoid.**—The head of the humerus lies beneath the coracoid process, in contact with it or at a variable dis-

tance—a finger's breadth at most—below it. The head may be displaced inward until three-fourths of its diameter lies to the inner side of the process (farther inward would be intracoracoid) or it may be simply balanced on the anterior edge of the glenoid fossa. The elbow hangs away from the side and the deltoid fullness of the shoulder is lost (Fig. 5). The axis of the humerus is seen to pass to the inner side of the glenoid fossa, and palpation reveals the absence of the usual bony resistance below the outer side

felt, will not participate in movements imparted to the shaft, and crepitus can usually be elicited.

In several cases the writer **transplanted a strip of bone**, periosteum-covered and 2 to 2.5 by 4 to 5 cm. in size, from the tibia under the loosened periosteum at the anterior glenoid margin so that it extended 0.5 to 1 cm. beyond the preexisting socket. In 2 cases in which 3 years had elapsed there was no recurrence. R. Eden (*Zentr. f. Chir.*, Aug. 14, 1920).

A portion of muscle from the posterior border of the **deltoid** may be detached and insinuated through the

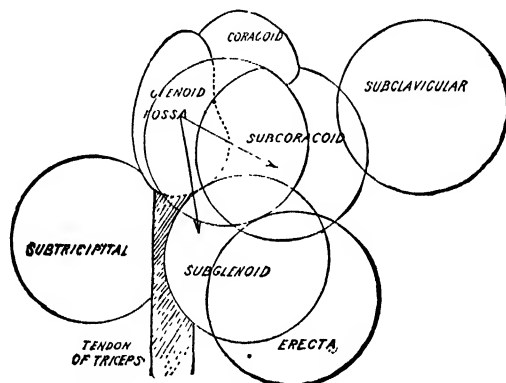


Fig. 4.—To show the range of positions that may be taken by the head of the humerus after primary displacement forward or downward in any of the directions between the arrows. (*Stimson, "Dislocations."*)

of the acromion, and the presence of an abnormal resistance below the coracoid process, or in the axilla, which partakes of rotary movements communicated to the arm. Voluntary movement is usually lost. Passively the arm can be abducted, but not so adducted that the elbow can touch the chest and the fingers rest on the opposite shoulder. Measurement in abduction shows shortening.

The diagnosis is usually easily made by finding the glenoid cavity empty, the head of the bone beneath the coracoid, and by eliciting the above-mentioned sign. If there be fracture of the anatomical neck the head, if it can be

quadrilateral space to an **attachment at the coracoid process**. Its nerve supply is retained, and in the danger position it actively supports the threatened capsule. A. Gibson (*Can. Med. Assoc. Jour.*, Mar., 1921).

The writer reports 22 successful results out of 24 cases of habitual dislocation treated by the **capsule operation**. T. T. Thomas (*Surg., Gynec. and Obst.*, Apr., 1921).

In the **reduction** of shoulder dislocation the writer first binds the recumbent patient's chest to the table with a towel, then raises the humerus vertically with his right hand, meanwhile manipulating the head of the bone into place with his left thumb on the head in the axilla. Malis (*Arch. f. klin. Chir.*, May 10, 1924).

The author has the patient lie on his side, with the arm hanging down and the head supported by an assistant. After allowing 2 or 3 minutes for the muscles to relax, he flexes the patient's elbow to a right angle, and makes downward pressure on the forearm with both hands, first rotating the arm outward and then inward. With a folded cloth under the scapula, the latter is held firm by the edge of the table, and reduction takes place quickly and easily. A little **morphine**

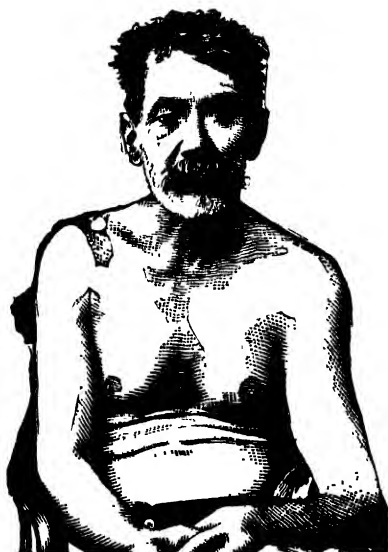


Fig. 5.—Subcoracoid dislocation of the left shoulder. (Stimson, "Dislocations.")

assists in the reduction. Dshanelidze (*Arch. f. klin. Chir.*, Aug. 29, 1924).

In recurrent dislocation, changes usually occur in the bone. X-ray findings afford a reliable and adequate picture of the bone conditions. Pilz (*Arch. f. klin. Chir.*, Apr. 2, 1925).

**Causes.**—Direct violence, by a blow upon the shoulder; indirect, as by a fall upon the hand; by leverage in forcible abduction and outward rotation; or by muscular action in any of the above ways.

**Pathology.**—The capsule is torn at its inner and lower portion, or, more rarely, stripped up, and with it may be

torn the circumflex nerve, the posterior circumflex artery, and subscapularis (Fig. 6). In "typical" cases the outer and upper portions of the capsule remain untorn and aid in determining the abduction. The supraspinatus, infraspinatus, and teres minor may be torn away (in decreasing order of frequency) from the greater tuberosity, or there may be avulsion of more or less of the tuberosity itself. With avulsion of the tuberosity the tendon of the long head of the biceps may slip to the outer side of the bone and oppose reduction (rarely). This tendon may also be torn. The head of the humerus may be bruised and ground by impact upon the glenoid margin, which, in turn, is splintered.

**Treatment.**—In uncomplicated cases reduction is usually easy by **Kocher's method**, as follows:—

The elbow is flexed to a right angle and pressed closely to the side; then the forearm is turned as far as possible away from the trunk—external rotation of the arm (Fig. 7). Maintaining the external rotation, the elbow is carried well forward and upward—flexion of the arm (Fig. 8)—and, finally, the hand swept over until it touches the chest—inward rotation (Fig. 9),—the elbow being simultaneously lowered. Anesthetics may or may not be necessary. If, after the "first movement," the head does not roll out in front of and below the acromion, the attempt will fail. Direct manipulation of the head may be of assistance.

If Kocher's method fails, traction downward and outward (never upward and outward, on account of the danger of lacerating the vessels) should be tried. After a long, steady pull, manual or elastic, the muscles may yield and allow the head of the bone to be pushed

back into place. Or, after a few moments of traction, the arm is forcibly adducted over the closed fist in the axilla (this is safer than the heel). If anesthetics are used, all of these forcible measures should be executed very cautiously.

The writer, in applying Kocher's method, dispenses entirely with the carrying of the hand toward the sound shoulder. The head of the humerus returns to the glenoid cavity during

Recent dislocations of the shoulder-joint can, as a rule, be reduced by the Kocher method or by direct traction; yet in certain unusual cases these methods fail. In 12 such cases, among which were several of long duration, the following method was successfully used by the author: A towel is looped around the inner side of the arm, just below the axillary folds, so that the free ends pass out at right angles to the long axis of the body. The patient is anesthetized,

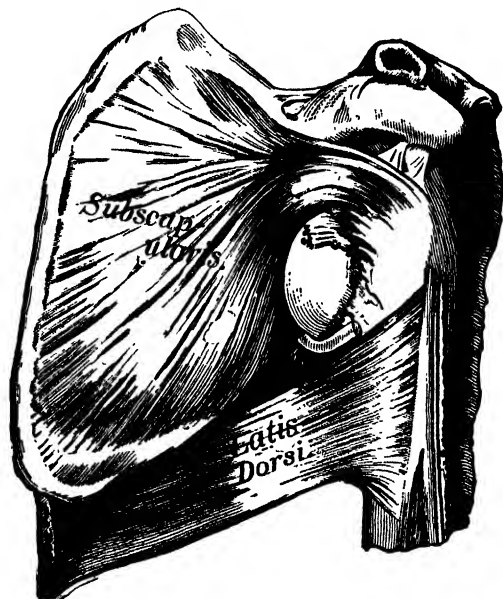


Fig. 6.—Subcoracoid dislocation on a cadaver, showing rupture of lower part of subscapularis. (B. Anger, in Stimson's "Dislocations.")

the preceding movement, that of the elbow. This movement should be carried out slowly, and brought to a stop at the point when maximal resistance is offered. Soon a slight jolt is felt, which signifies that the head has re-entered the glenoid fossa. An essential point consists in manipulating gently, to avoid causing pain and consequent firm contraction of the muscles. The patient should preferably be kept ignorant of the fact that reduction is about to be performed, voluntary resistance being thereby eliminated. M. G. Gallois (Bull. méd., Dec. 11, 1909).

an assistant grasps the forearm on the injured side and applies extension strongly, parallel to the long axis of the patient's body. Simultaneously, the anesthetist makes counter-extension with his fingers in the axilla, while the surgeon pulls the free end of the loop outwardly. P. Turner (Pract., ci, 75, 1918).

The usual treatment of dislocation of the shoulder by fixation of the arm to the side is irrational and unsuccessful, resulting in limitation of abduction and osteoarthritis. In rectangular abduction the rent in the capsule is closely coaptated, whereas in ad-



duction the capsule is crowded together in a crinkly lump and coheres in that position. The arm is no more likely to redislocate when placed in abduction than when tied to the side, and the resulting movements are much better and are obtained much more quickly and less painfully. All patients treated by abduction were able to raise the arms well above the head. A. H. Todd (*Pract.*, Mar., 1920).

Prolonged traction upon the abducted arm, the patient lying upon the opposite side (Malgaigne), or with the body horizontal and the arm dependent (Stimson), as in Fig. 10, will, in a recent case, often cause reduction in a few minutes.

If judicious attempts at reduction by these methods fail, even under anesthesia, an open arthrotomy should be done for the purpose of discovering and removing the obstacle.

In intracoracoid dislocations the head is displaced farther inward and



Fig. 7.—Kocher's method of reduction by manipulation. First movement, out-ward rotation. (Oeppli, "*American Text-book of Surgery.*")

the symptoms are those of the subcoracoid, except that the head of the humerus is felt farther displaced and the shoulder is more flattened. The arm may be fixed in horizontal abduction. The cause of this particular dislocation is, as a rule, an unusual

amount of laceration of the capsule and subscapularis, which allows the head of the bone to pass farther inward. Reduction by outward traction is easy unless the subscapularis or torn capsule intervene. In such cases operation is the only recourse.

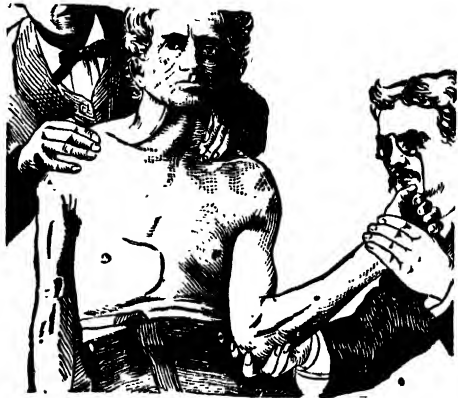


Fig. 8.—Kocher's method of reduction. Second movement, circumduction of elbow. (Oeppli, "*American Text-book of Surgery.*")

Nothing is worse for a shoulder luxation than immobilization in the usual sling, and the writer advises immediate massage and movement of the joint, which should never be delayed beyond twenty-four hours. Yvert (*Presse méd.*, June 17, 1911).

The writer seizes with his right hand the hand of the dislocated member, which is thrown about the operator's neck and with the free left hand directs without difficulty the head of the humerus, extending, counterextending, and reducing at will. The operator is thus able to apply extension, counter-extension or reduction and needs no assistant. Angelvin (*Semaine méd.*, March 20, 1912).

In subclavicular dislocations the same forces acting more energetically force the head of the bone farther in.

Downward dislocations include all cases in which the head of the bone lies below the glenoid fossa. In subtricipital dislocation, of which one case is recorded, the head of the humerus was

displaced secondarily backward and upward behind the long head of the triceps.

*Subglenoid Dislocations.*—The symptoms are those of subcoracoid dislocation; but abduction and flattening of the shoulder more marked. The head of the bone is palpable below its socket. The upper part of the greater tuberosity is habitually torn away. The usual cause is forcible abduction followed by rotation or impulsion.

The treatment indicated here is traction in moderate abduction with direct pressure.

*Luxatio Erecta.*—Very rarely, by forcible elevation of the arm, the head of the bone is displaced so far downward that the extremity maintains its erect position. It is reduced by upward traction until the head falls into place.



Fig. 9.—Kocher's method of reduction. Third movement, inward rotation and lowering of elbow (Oeppi, "American Text-book of Surgery.")

*Posterior Dislocations.*—The two varieties differ only in the extent of displacement.

*Symptoms.*—The arm is adducted and rotated in, the elbow being directed slightly forward. The shoulder is flat

in front and full behind (where the head of the bone may be felt). Passive motion is restricted; voluntary motions absent.

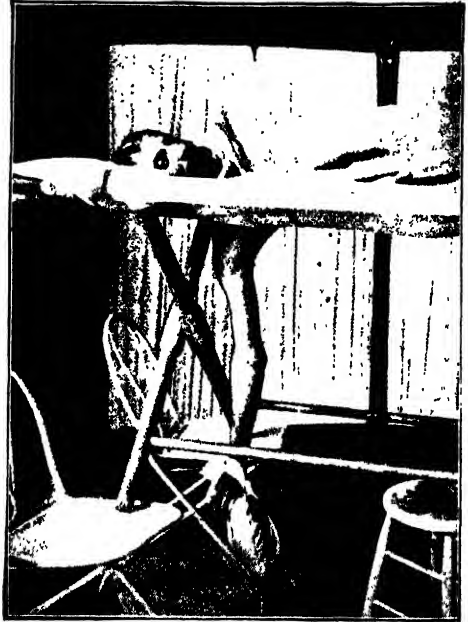


Fig. 10.—Reduction of anterior dislocation of the shoulder. (Stimson.)

The cause is direct pressure outward and backward, or the pressure exerted in the same direction along the adducted and inward-rotated humerus.

The outer side of the capsule is torn and the external and internal scapular muscles more or less lacerated or avulsed with fragments of the tuberosities. The head of the bone lies on the outer edge of the glenoid fossa, or farther back beneath the spine of the scapula, or on the infraspinatus.

*Treatment.*—Reduction is accomplished by traction and direct pressure forward. Avulsion of the subscapularis makes recurrence probable. Unreduced dislocations backward are accompanied by an unusual amount of disability.

*Upward Dislocations.*—These are ex-

tremely rare. The head of the bone is forced upward between the coracoid and acromion, usually to above the clavicle. The arm is almost immobilized in adduction and slight extension. Reduction may be effected by downward traction.

*Complications of Dislocations of the Shoulder.*—Compound dislocations are very rare, and are commonly caused by direct violence. The skin wound is usually in the axilla. Aside from complications which may exist not dependent on the dislocation, the great dangers are from laceration of the main arteries (frequent) or nerves (unusual) and from suppuration. The treatment consists of enlarging the wound until the extent of damage can be fully appreciated and, as far as possible, repaired. Meanwhile the wound should be thoroughly irrigated with "normal" salt solution. The dislocation may now be easily reduced. In most cases thorough drainage should be provided for, and in some cases it may be advisable to excise the head of the humerus to this end to oppose ankylosis.

Fractures of the various bony prominences of the scapula and humerus have commonly a purely pathological importance. Fractures of the anatomical or surgical neck of the humerus are important, but often difficult to diagnose without the aid of the X-ray, which should always be invoked. The diagnostic points of fracture of the anatomical neck are the recognition of the head in the axilla and its failure to move with the shaft, the maintenance of nearly normal range of motion, and the normal position of the greater tuberosity. Crepitus may sometimes be elicited. In fracture of the surgical neck the signs are quite the same, except that the tuberosity is displaced with the head, and, with it, fails to

move with the shaft, and crepitus is more easily elicited. In either case the upper fragment may be reducible by direct manipulation. This failing, if the fragments can be approximated, the arm may be immobilized for three or four weeks in an appropriate position with the hope of obtaining union and effecting reduction at the end of that time by manipulation. But the better plan is probably to do an open arthrotomy and remove the upper fragment, except in such fractures of the surgical neck as can be reduced, and to this end the use of a strong right-angled hook inserted into a hole drilled at the lower end of the upper fragment may be of great service (McBurney). The metal skid of Kocher is of the greatest value for sliding and guiding the articular head into its socket. Or a fairly useful false joint may sometimes be obtained at the point of fracture.

#### **Injuries to Vessels and Nerves.**—

The axillary itself is very rarely ruptured, and, hence the radial pulse may persist, even though there be serious damage to the smaller arteries about the joint. This damage is usually due to ill-advised attempts at reduction, and is recognized by the rapid extravasation of blood down the arm and into the axilla. Treatment is by pressure, ligature of the axillary at the rupture or of the subclavian, or disarticulation at the shoulder. The mortality is very high. The circumflex nerve is sometimes torn, with a resulting temporary or permanent disability of the deltoid and anesthesia of the shoulder.

**Treatment of Old Unreduced Dislocations.**—If the dislocation cannot be reduced after loosening adhesions by forcible (yet judicious) rotation and

traction, operation is advisable for reduction by division of the soft parts, or for excision of the head of the bone. A very serviceable joint may be obtained by the latter method; but as the line of division of the bone runs below the tuberosities, rotation is practically lost.

On examining 32 cases of fresh and old dislocations of the shoulder-joint with their X-ray plates, the writer noted that the most common complication was a fracture or stripping off of the greater tuberosity. Out of these cases 19 showed a fracture of the greater tuberosity and 3, fractures through the anatomical neck. The treatment is not always easy, because of the marked obstruction to motion. The X-ray is of the utmost importance in determining between simple dislocation or dislocation with fracture. The operative cases are those in which a large fragment is torn off and displaced so that the normal position of the arm will not reduce the fragment to a point near that from which it was detached. In such a case the fragment is reduced by open operation and held in place by ordinary wire nails. Smaller fragments which are torn off and carried into the joint, where they offer obstruction to motion, are removed by open operation. Exostoses which form as a result of stripping of the periosteum are also removed as above. In all cases where an operation has been performed for removal of obstruction to the outward and upward motion the arm is put up as high as possible and retained in this position by a plaster cast, which should be cut at the end of  $2\frac{1}{2}$  to 3 weeks, when the patient should receive a slight amount of passive motion. F. F. Henderson (Boston Med. and Surg. Jour., Oct. 18, 1917).

*Habitual or recurrent dislocations* may result from an avulsion of the greater or lesser tuberosities in the tearing of the muscles from their processes; from fractures involving the glenoid cavity, or from relaxation of

the capsule and ligamentous structure. The treatment consists in: (1) Re-attaching the divided muscular tendons or bony processes by suture or by metal, bone or ivory nails; (2) deepening the glenoid cavity and flattening it by removing part of its posterior edge (Hildebrand); (3) transplanting muscles (*e.g.*, a pectoralis major flap) to give added support, and (4) reefing the capsule or stimulating the formation of adhesions by packing the wound down to an opening in the capsule (Thomas).

In recurrent dislocations of the shoulder capsulorrhaphy is curative in most cases. An extreme measure, which would be justifiable only after the failure of other methods, is the making of an arthrodesis with ankylosis of the humeral head to the scapula with the arm at a right angle. Resection of the head of the humerus is unjustifiable. In capsulorrhaphy the capsule is exposed by an incision along the anterior axillary fold with the arm in abduction, the pectoralis major is retracted strongly, and the capsule is reached below the tendon of the subscapularis. The capsule is incised and three or four fold No. 2 chromic gut mattress sutures are placed so that their tightening will make the two cut edges overlap. To aid in the overlapping the arm is rotated and the sutures are drawn up and tied. M. S. Henderson (Jour. Amer. Med. Assoc., Jan. 5, 1918).

Description of a new method used successfully in 5 cases. A suspensory ligament of fascia lata or silk is passed through a drill hole close to the head of the humerus from before backward, emerging posteriorly through the greater tuberosity. The posterior end is passed under the deltoid muscle, up anteriorly to the outer end of the clavicle, then over and behind it, and finally down to the starting point. The fascial ligament is drawn tight with the arm at an angle of 45 degrees, the ends being overlapped and sutured.

The arm is supported by a sling and kept at rest for 6 weeks. T. L. Sandes (Brit. Med. Jour., ii, 321, 1921).

The writer either introduces a **bone graft** between the tip and base of the coracoid process, or **lengthens the coracoid process** by splitting it lengthwise and sliding down the  $\frac{1}{2}$  so as to prolong it by 3 centimeters. Oudard (Jour. de chir., Jan., 1924).

The writer recommends **crucial capsular plication**, transverse and vertical, as promoting uniform contraction of the capsule. W. L. Keller (Ann. of Surg., Jan., 1925).

**Dislocations of the elbow** stand second in order of frequency, and are most common in persons under 25. Among the great variety of forms of dislocations of both bones, the backward are by far the most frequent.

The divisions and subdivisions are as follows:—

- |   |   |  |
|---|---|--|
| Dislocation of Both Bones of the Fore-arm | { | 1. Dislocations backward:<br>and outward.<br>and inward.   |
|   |   | 2. Lateral dislocations:<br>Incomplete { inward.<br>outward.   |
|   |   | Complete -- outward.   |
|   |   | 3. Forward dislocations:<br>Incomplete (first degree).<br>Complete (second degree).<br>With fracture of the olecranon.         |
| Dislocations of Ulna Alone                | { | 4. Divergent dislocations.<br>Anteroposterior.<br>Lateral.   |
|   |   | Backward and Upward { Incomplete (first degree).<br>Complete (second degree).  |
| Dislocations of the Radius Alone          | { | Backward and Outward (behind the radius).<br>Inward (one case).  |
|   |   | 1. Backward.<br>2. Outward.<br>3. Forward.<br>4. By elongation (the subluxation of children).<br>5. With fracture of the ulna. |

#### *Dislocations of Both Bones Backward.*

—The inward and outward subvarieties are of no practical importance.

**Symptoms.**—The elbow is swelled and partly flexed. The olecranon may be felt displaced backward from the epicondyles and the head of the radius may be recognized behind the external epicondyle as a bony point which rotates with the forearm. The trochlear surface may be prominent in the bend of the elbow; the tendon of the biceps behind. Passive flexion and extension are moderate. There is abnormal lateral mobility in full extension.

The cause is most commonly a fall upon the outstretched hand forcing the two bones backward. The coronoid process of the ulna is either broken or lifted over the trochlear surface by hyperextension or by abduction, which increases the normal outward deviation of the forearm and a twist which swings the process downward and then backward.

**Pathology.**—The internal lateral ligament is torn, and the external one either torn or stripped away with the periosteum from the external condyle. Hence, in old dislocations reduction is effectually prevented by the mass of callus that forms beneath this elevated periosteum behind the external condyle. The front of the capsule is torn, the epitrochlea (internal epicondyle) may be broken by muscular pull, or the muscles attached to it may be ruptured. Fractures of the head of the radius and coronoid process are rare. The latter, however, does not interfere with the action of the brachialis anticus, as that muscle is attached to the base of the process: a part not interested in the fracture.

**Treatment.**—Forcible flexion is to be condemned as unscientific and less likely to succeed than pressure on the dislocated bones combined with traction of the forearm in full extension or hy-

**perextension.** Usually the dislocation is easily reduced. Sometimes anesthetics are necessary. After reduction the limb should be immobilized by bandages and a sling for about three weeks, after which massage and mild active motion will gradually remove the stiffness. Early passive motion will not hasten the result, and may even increase the excessive production of callus, which, in children, sometimes goes on even after reduction, and may cause serious limitation to the motion of the joint.

In old-standing dislocations of both arm bones backward, reduction without a cutting operation is very rarely successful, and is often attended by very serious injury to the bones, especially in young subjects. Section of the olecranon allows easy reduction, and the fixation of the detached piece by a screw gives an ideal result. Operation from the posterior aspect of the joint is anatomically sound, as all the important structures, except the ulnar nerve, lie in front separated from the area of work by the brachialis anticus. No lateral incisions can give the power to deal with a shortened triceps, which will prevent reduction no matter how freely the lateral ligaments are divided. Fixation by a screw instead of by wiring saves much delay and avoids undue exposure of the periarticular tissues. M'Ardle (Dublin Jour. of Med. Sci., March, 1912).

**Lateral Dislocations.**—Incomplete dislocations in either direction are said to be frequently overlooked or mistaken for fractures. The cause of lateral dislocations is usually a fall upon the hand by which the normal outward angle at the elbow is increased by tearing of the internal lateral ligament and a downward movement of the ulna, directly away from the trochlea. The head of the radius then glides either outward or inward, as the case may be, the ulna accompanying.

*In incomplete inward dislocations* the forearm is pronated and slightly flexed, its long axis parallel to and a little to the inner side of that of the arm. The olecranon and external condyle are prominent, and the head of the radius can be felt displaced inward, resting below the trochlea (the greater sigmoid cavity of the ulna embraces the epitrochlea). Flexion and extension are but little interfered with. Reduction is made by traction and direct pressure. In unreduced cases there is very little disability, and operative interference is probably inadvisable.

*Incomplete Outward Dislocations.*—The forearm is pronated and slightly flexed, and its long axis is to the outer side of and parallel to that of the arm or else in abduction. The ulna is displaced so that the central ridge of the greater sigmoid cavity has passed beyond the outer rim of the trochlea; the radius lies partly below or entirely beyond the external condyle. The internal condyle and olecranon are prominent.

**Treatment.**—The ridge of the sigmoid cavity must be unlocked from the groove between the trochlea and capitellum. This is done by traction or hyperextension (or by abduction, if the head of the radius rests below the external condyle and can be used as a fulcrum). Then the bones are pushed easily into place. The broken epitrochlea may lodge in the groove of the trochlea and effectually prevent reduction. Even if the dislocation be not reduced, the joint may be quite useful.

Complete outward dislocation occurs in three forms. In the simplest form the bones of the forearm are displaced directly outward, the inner edge of the olecranon resting against the outer side of the external condyle. If, now, the forearm is flexed and strongly pronated,

the second form (subepicondylar) is produced, in which the anterior surface of the ulna looks inward and its sigmoid cavity embraces the outer side of the external condyle, while the radius lies above it, with its head in front of the epicondylar ridge. In the third form (supraepicondylar) the dislocated bones are moved still farther upward and backward, so that their articular surfaces lie external to and behind the supinator ridge. Reduction is usually easy, owing to the extensive laceration of the ligaments; but, even if unreduced, the elbow remains fairly strong and mobile.

*Forward Dislocation.*—This rare injury is usually caused by direct trauma at the back of the flexed elbow. The olecranon was broken in about a third of the cases, and in such the violence is received on the posterior surface of the ulna. If this is the case, the ulna and radius are displaced forward and upward in the anterior surface of the humerus; but, if the olecranon remains intact, it may rest on the trochlea, or, the triceps being torn away, it may pass to the front of the humerus. Reduction by traction appears to have been easily accomplished.

*Divergent Dislocations of the Radius and Ulna.*—In the anteroposterior variety the ulna lies behind and the radius in front of the humerus; in the transverse the ulna is displaced inward and the radius outward. The usual cause seems to be abduction followed by internal rotation and impulsion. Reduction has failed in one-fourth of the cases.

*Dislocation of the Ulna Alone.*—The forearm is usually extended and adducted. Flexion is painful; rotation free. The trochlea is prominent in front and the olecranon behind, while the head

of the radius remains in place. The cause of the injury appears to be hyperextension or abduction, followed by adduction and inward rotation. The rational method of reduction is by supination, abduction, and hyperextension (von Pitha).

*Dislocation of the Radius Alone.*—Of the dislocations backward, outward, and forward the last is the most frequent, being, in fact, of not unusual occurrence in connection with a fracture of the shaft of the ulna from a fall upon the hand. The head of the bone is displaced upward in front of the external condyle. The orbicular and anterior ligaments are torn. Abduction is possible, while supination, flexion, and adduction are all limited. Adduction and pressure appear to be the best methods of reduction; but the orbicular ligament may be interposed and require operative interference.

The backward and outward dislocations are very rare. They necessitate a fracture of the ulna or a rupture of the interosseous membrane.

The downward dislocation (dislocation by elongation, subluxation of young children) is of frequent occurrence. The clinical history is quite characteristic: a child, usually under 3 years of age, is pulled by the hand; it cries out, and refuses to use the limb, which hangs with the forearm partly flexed and pronated. The region of the head of the radius is sensitive to pressure, and sometimes an interval can be felt between the radius and the condyle. All passive motions, except supination, are free. On forcible supination a slight click may be felt and the symptoms are at once relieved. Duverney's theory of downward displacement with interposition of the annular ligament is most in accord with the facts.

In recent cases secure reduction of the dislocated radial head, by arthrotomy and capsulorrhaphy if necessary. As Kirmisson says, in such injuries the dislocation is everything, the fracture is nothing. When reduction is secured the fracture almost invariably will fall into good position. If it does not, it may be fixed by a suture or plate. In old cases with the ulna united attempt reduction of the dislocation by arthrotomy and retain the radius in place by capsulorrhaphy. If reduction after arthrotomy proves impossible, as it may if the ulna has united in bad position, it is better to excise the head of the radius than to interfere with the ulna, unless the deformity in the ulna is very extreme. In such cases osteotomy of the ulna may be done. In old cases with non-union of the ulna expose the ulnar fracture first, and after freeing the fragments secure reduction of the dislocation by arthrotomy if necessary, including capsulorrhaphy; then treat the ulnar fracture as if no dislocation had existed. In cases with musculospiral paralysis excision of the radial head failed to secure a good result in one case (Zschock), and there is no evidence that reduction and capsulorrhaphy would not have been successful in two others (Albertin, Kammerer) in which excision was done. A. P. C. Ashhurst (*Annals of Surg.*, Oct., 1912).

**Old Unreduced Dislocations of the Elbow.**—Adhesions and new bone formation very soon immobilize the joint. If this immobilization occurs in extension, the position may be improved by forcible flexion, with or without fracture of the olecranon. A more accurate method, however, and one likely in many cases to afford fairly good functional results, is arthrotomy. The chief obstacle to reduction will be found to be the new bone formed at the back of the external condyle. This may be removed and adhesions divided through two lateral incisions.

The writer found in 3 cases that an otherwise irreducible backward luxation of the elbow corrected itself spontaneously when the man hooked his elbow over the rung of a ladder, the highest he could reach, and bore his weight on it. The relaxation of the triceps is probably responsible for this as the elbow is hooked high up, the man leaning against the ladder as he stands sideways at the foot. Verny (*Arch. de méd. et de Pharm. Milit.*, Apr., 1918).

**Dislocations of the Lower Radio-Ulnar Joint.**—The ulna is spoken of as the dislocated bone. It may be dislocated forward or backward. The latter

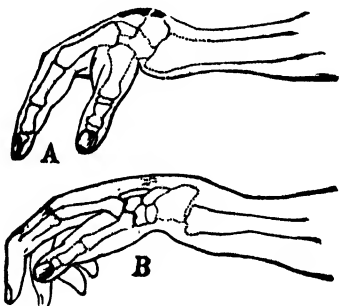


Fig. 11.—Diagrammatic, to indicate the deformity in A, dislocation of the wrist backward, and B, Colles's fracture of the radius. (Stimson.)

variety is caused by exaggerated pronation, and the former by direct trauma. Both are easily reduced.

**Dislocations of the Carpus from the Radius.**—These may be complete or incomplete; forward, backward, or outward. In the incomplete form the cuneiform maintains its relations to the triangular fibrocartilage, while the scaphoid and semilunar are dislocated from the radius. In one case the semilunar alone was not displaced (backward). These dislocations may be complicated by fracture of the anterior or posterior ("Barton's fracture") lip of the radius; but this in no way complicates the treatment and is a purely secondary matter.



The more common Colles fracture of the lower end of the radius was long confounded with backward dislocation. The differential diagnosis is easily made by attention to the relations of the styloid process of the radius with that of the ulna and with the projecting mass on the back of the wrist (Fig. 11). Reduction in either case is made by dorsal flexion and direct pressure, and after reduction the differential diagnosis is easy. The spontaneous forward dislocation of Madelung occurs slowly in adolescents as the result of absorption of the anterior part of the articular surface of the radius. The ulna is prominent; dorsal flexion is limited.

[According to Marson, Madelung has been shown to have been in error, in that there is no luxation, but a diaphyseal or epiphyseal incurvation of the radius. The disease is, therefore, a curved radius. The radiocarpal connection remains normal.]

#### Dislocation of the Carpal Bones.—

Dislocations have been reported of each of the carpal bones, except the cuneiform. If the bone cannot be replaced or causes annoying symptoms, it had better be removed.

In early cases of dislocation of the semilunar bone an attempt at bloodless reduction by over-extension and the Thomas wrench under complete anesthesia should be made. The reduced semilunar should be held in place by fixation in extreme flexion. Physiotherapy should be used early and continued until function is restored. Old, intractable dislocations or severe fracture dislocations should be excised. W. G.

Stern (Jour. Amer. Med. Assoc., lxxv, 1389, 1920).

A few dislocations of the second row of carpal bones upon the first have been reported.

#### Carpometacarpal Dislocations.—

The first metacarpal is the one most

commonly dislocated; the dislocation is incomplete and usually backward. The base of the dislocated bone forms a distinct prominence on the back of the hand; this is readily reduced, but as readily recurs. To prevent recurrence, extension of the finger (and also abduction, if it be the thumb) and direct pressure on the head of the bone must be maintained by a dorsal splint for one or two weeks.

Dorsal metacarpophalangeal dislocations are generally caused by a fall on the outstretched hand; more rarely, by direct violence or by trac-

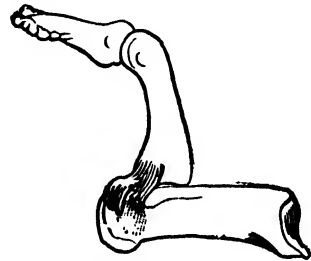


Fig. 12.—Simple complete dislocation of the thumb. (Farabeuf.)

tion from scars. Diagnosis and replacement are generally easy, but occasionally reposition is made more difficult by the interposition of a piece of capsule, a joint ligament, or a flexor tendon. In some cases operative reposition is necessary. Dislocations of the toes are more rare than dislocations of the fingers, but more frequently compound and combined with fractures than those of the fingers. W. Strube (Beitr. z. klin. Chir., cxx, 646, 1920).

#### Dislocations of the Thumb and Fingers.—Metacarpophalangeal Dislocations of the Thumb.—

Lateral (one case) and forward dislocations present no especial points of interest. The latter are easily reduced by hyperflexion and traction. Backward dislocation may be incomplete, complete, or complex. Incomplete backward dislocation may

be produced voluntarily by many young persons. It is reduced at will. In the complete form the phalanx is carried backward and upward on the dorsum of the metacarpal, usually by forced extension; the anterior ligament is torn away from the metacarpal bone and drawn backward with its sesamoid bones along, and even past, the articular surface of the head of the metacarpal, while the tendon of the long flexor slips to one side of the head, usually the inner, although it may exceptionally remain in place. The first phalanx is in extension at a right angle, the terminal phalanx in flexion, and the head of the metacarpal prominent in the thenar eminence (Fig. 12).



Fig. 13.—Complex dislocation. (Parabeuf.)

In the complex form (produced from the complete by forced flexion of the thumb) the glenoid ligament, and the two sesamoid bones with it, are turned upward so as to lie between the phalanx and the head or dorsum of the metacarpal. The thumb is in straight extension, parallel and posterior to the metacarpal; its base can be felt as a prominence behind, and the head of the metacarpal protrudes in front. The sesamoid bones stand at a right angle to the articular surface of the phalanx, and cannot be folded under it, thus offering a great—often insurmountable—obstacle to reduction. The essential point of reduction, therefore, is to avoid the transformation of the complete into the complex form. The extension must be maintained or even increased and the thumb pressed bodily downward until

the anterior edge of its base, following the glenoid ligament, overlaps the articular surface of the metacarpal, when it can be turned into place by flexion. If this fails, a combination of rotation with the downward pressure may succeed: a sort of unbuttoning of the head of the metacarpal from the grasp of the glenoid ligament and the attached heads of the short flexor. If, however, the dislocation has become complex by the interposition of the glenoid ligament, the same method may yet succeed; but much more forcible downward traction is necessary to carry the edge of the ligament over the end of the metacarpal bone ahead of the phalanx before instituting flexion. If all manipulations fail, the joint must be opened through a longitudinal anterior incision, and the center of the glenoid ligament nicked to allow it to be drawn over the head of the metacarpal.

*Metacarpophalangeal dislocations of the fingers* resemble those of the thumb, save for usual absence of sesamoid bones.

*Dislocation of the phalanges* may occur in any direction. Reduction is usually easy, though possibly the thick anterior ligament may be interposed.

**Dislocations of the Pelvis and Coccyx.**—Pubic and sacroiliac dislocation occurs with fracture of the pelvis, the symptoms and treatment of which it does not materially complicate.

The coccyx may be dislocated forward or backward. The pain is usually intense. Diagnosis is made by rectal touch. Manual reduction should always be attempted.

The condition is rare except in neurasthenic women. Fibrous or bony ankylosis may occur, preventing reduction. For the relief of the pain local injec-

tions of 2 per cent. phenol, or of 80 per cent. alcohol, or coccygectomy may be tried. Often neurasthenic symptoms persist despite operation.

**Dislocations of the Hip.**—These form from 2 to 10 per cent. of all dislocations; they occur at all ages and are more common in men than in women. The head of the femur may leave its socket in any of the four principal directions, after which it assumes various positions by secondary displacement. In "typical" dislocations the Y-ligament remains untorn and determines the characteristic attitude of the limb (Bigelow). Compound dislocations are rare. The varieties are as follows:—

- |   |   |  |
|---|---|--|
| Dislocations  | { | "Typical" dorsal (comprising the iliac and "ischiatric," and those "upon the dorsum ilia" and "into the ischiatic notch"). |
| Backward  |   |  |
| Dislocations  | { | Anterior oblique.<br>Everted dorsal (comprising the "supraspinous" and some of the "supracotyloid").                       |
| Backward  |   |  |
| Dislocations  | { | Obturator.<br>Perineal.  |
| Downward and Inward   |   |  |
| Dislocations  | { | Ilio-pectineal.<br>Pubic.<br>Intrapelvic.  |
| Forward and Upward  |   |  |
| Suprapubic  |   |  |
| Dislocations directly upward (supracotyloid or subspinous). |   |  |
| Dislocations downward on the tuberosity of the ischium.     |   |  |

**Backward Dislocations.**—The dorsal form is by far the most common of the dislocations of the hip. The thigh is adducted, rotated inward, and more or less flexed; so that the knee rests upon the front of the opposite thigh when the patient is recumbent, and there is apparent shortening (Fig. 14). The upper and outer part of the thigh is broadened, and the trochanter is above Nélaton's line (a line drawn from the antero-superior spine of the ilium to the tuberosity of the ischium). The head of the femur may be obscurely felt in the buttock.

The actual shortening cannot easily be determined on account of the difficulty of placing the two limbs in symmetrical positions. Voluntary movements are lost; passive flexion and adduction alone are possible.

The characteristic position and limitation of motion readily distinguishes the dislocation from a fracture of the neck of the femur.

**Etiology.**—The dislocation is usually produced by violence transmitted along the shaft of the femur while the thigh is flexed, adducted, and rotated inward, or the head of the bone may be thrown out of place by exaggerated adduction, inward rotation, and slight flexion, or, again, the dislocation may result secondarily from an obturator dislocation by the same three motions.

**Pathology.**—The head of the bone usually tears through the capsule low down behind, passes below and then upward behind the obturator, and rests finally on that muscle close behind the acetabulum, or, more rarely, it leaves its socket higher up, pushes the obturator ahead of it outward or upward, and lies on the edge of the acetabulum itself. The capsule is irregularly torn behind, the ligamentum teres is ruptured, the quadratus femoris and gemelli are usually torn, the two obturators and pyri-forms less frequently. Rarely the head of the bone rests on the great sciatic notch or the dorsum ilii. The edge of the acetabulum may be broken.

**Treatment.**—The surgeon must endeavor to relax the Y-ligament and other untorn portions of the capsule, to bring the head of the bone opposite the rent in the capsule (if necessary), and then to lift or pry it into place. To do this the patient is laid flat on his back and the pelvis steadied by an assistant or by the surgeon's foot. The patient's

knee is then flexed at a right angle, the thigh rotated inward and flexed to or a little beyond a right angle, and then lifted bodily upward, rotated a little outward, and extended in abduction. The lifting and outward rotation should replace the bone with a distinct jump.

Or the patient may be laid on his face on a table whose edge comes just above the groin so as to leave the lower extremities dangling. The sound limb is now held horizontally by an assistant, and the dislocated one allowed to hang vertically downward. The surgeon grasps the ankle of the dislocated limb, flexes the knee to a right angle, and, while diverting the patient's attention, swings the limb gently from side to side. Under the influence of gravity the mus-

and adduction, aided by direct pressure on the great trochanter.

If the limb is too strongly flexed or too soon rotated outward the dorsal dislocation may be transformed into a thyroid one. If this occurs, the dislocation must be restored to its original form by

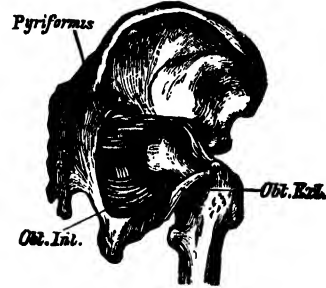


Fig. 13.—Dislocation below, and then bending and above, the obturator internus. (Stimson.)

reversing the movements: flexion in abduction and outward rotation, followed by adduction and rotation inward.

In reviewing the ultimate results observed in 21 cases of hip luxation, some reduced by ordinary methods soon after the accident, others treated later by open operation, the writer concludes that the late prognosis in these cases is not entirely favorable. Although occasionally the subsequent trouble may arise from osseous abnormalities existing before or as the result of the accident, and which might have been avoided by routine use of the X-rays in these cases, the disturbance is usually due to imperfect restoration of the soft parts surrounding the joint. In adults, one should always be apprehensive of a posttraumatic deforming arthritis, which may appear at a long interval after the accident. The best way of preventing this and other untoward results is to keep all these patients under treatment, after the dislocation, for a longer time than has hitherto been the custom. In reducing hip luxations, he advises the following maneuver, which permits of easy reduction, even where the patient's limb is unusually massive: With the patient anesthetized and lying on a mattress,



Fig. 14.—Dorsal dislocation of femur. (Ooeper.)

cles soon relax and the bone may slip into place of itself or aided by a sharp, quick pressure downward on the calf.

If these methods fail, ether should be administered and reduction attempted several times by the first method. Failing again, try traction in slight flexion

the thigh is flexed to liberate the femoral head, and the operator's knee placed under that of the patient. Holding the patient's leg below the knee and at the ankle, the operator then applies force to it just as a laborer would lift a heavy shovelful of earth. Roux (*Revue méd. de la Suisse Romande*, Jan., 1913).

*Everted Dorsal Dislocations.*—If the outer branch of the Y-ligament is ruptured, the limitation to abduction and outward rotation is, in great part, removed, and the head of the bone is free to rise higher than before. Hence, when this rupture occurs, if the head remains behind the acetabulum only slight flexion and adduction persist, while, if it has moved upward and forward near to or above the anteroinferior spine of the ilium (in which position it can be felt), there will be extension, abduction, and slight outward rotation: the so-called everted dorsal. Reduction is effected by converting the dislocation into the common dorsal form and treating it as such.

*Anterior Oblique Dislocation.*—In Bigelow's one reported case the head of the bone was high above the acetabulum and the limb crossed the opposite thigh, everted, and with the knee extended. Reduction as for everted dorsal dislocation.

*Dislocations Downward and Inward.*—In both the obturator—or thyroid—and perineal varieties the head escapes through a rent in the lower and inner part of the capsule to lodge on the obturator foramen, or to proceed farther and rest on the perineum. In either case the limb is flexed, abducted, and rotated outward. It cannot be extended and can only be adducted after flexion. The limb is shortened, the trochanteric region flattened, and adductors tense. The head of the femur may sometimes

be felt on the foramen, always if it is in the perineum, in which latter case the abnormality of the position of the limb is much greater. Several patients are reported to have walked immediately after receiving a thyroid dislocation.

The common cause is violence received on the back of the pelvis while the thigh is somewhat flexed and abducted; but it may be extreme abduction alone. In perineal dislocations the laceration of the soft parts must be extensive.

Reduction is made by flexion of the hip to a right angle, traction with adduction, and then inward (or outward) rotation while lowering the knee. Manipulation may succeed with no rotation at all.

*Dislocations Upward and Forward, and Inward and Forward (Suprapubic).*—The limb is extended, markedly everted, and slightly abducted. The head of the femur is commonly to be felt in the groin (iliopectineal form) or may be above the pubes. The psoas-iliacus and the great vessels are stretched across the head or may be ruptured. The head of the bone may have left the socket at its upper and inner part by hyperextension, or by abduction and outward rotation, or the dislocation may be secondary to an obturator dislocation.

*Reduction.*—The head is to be drawn downward past the pubic ramus by direct traction in the axis of the limb as it lies; then flexion is instituted while pressure is made against the head to prevent its moving upward again; and, finally, inward rotation replaces the bone.

*Dislocations Directly Upward (Supracotyloid).*—In the few recorded cases the head had been forced directly upward and lay just beneath the antero-

inferior spine of the ilium. The limb was everted and abducted. Some of the patients have been able to walk with a limp.

These cases bear a close resemblance to everted dorsal dislocations. No definite rules for reduction have been laid down.

*Dislocation Downward upon the Tuberosity of the Ischium.*—This dislocation is very rare because of the case with which it may be converted into a dorsal or thyroid dislocation. The thigh is sharply flexed and abducted. Reduction is easy by traction in flexion.

*Complications of Dislocations of the Hip.*—Compound dislocations are very rare.

Injury to the femoral vessels may occur in forward and inward dislocations and should immediately be treated by operation and suture.

Fracture of the neck of the femur is usually caused by overzealous attempts at reduction. Operative reduction with the Kocher skid and fixation of the fragments by a screw of bone or metal passed through the neck of the bone from the trochanter is to be done; otherwise, ankylosis with the limb in a favorable position is the best that can be hoped for, except possibly in the young, when excision of the head of the bone may give some useful motion.

Traumatic luxation of the hip is a rare lesion during infancy and the early years and is proportionately more frequent in later years. It is more frequent in the male sex. Its rarity is not explicable by the greater frequency of femoral fracture, since this includes only diaphyseal fractures which generally have a pathogenesis different from luxations; it is rather in strict relation with the physiologic peculiarities of the joint.

Iliac luxations are the most frequent variety. The period of reduction is shorter than in the adult owing to the more active proliferation of tissues and easy periosteal detachments.

Reduction can always be easily effected in recent luxation when an exact diagnosis guides the reduction maneuvers. Plaster apparatus is preferable to traction to secure the reduced position and eliminate the danger of re-luxation. G. Roello (Clin. Chir., Milano, xxiv, 1480, 1916).

*Treatment of Old Unreduced Dislocations.*—Both forcible reduction and reduction by arthrotomy have yielded, in the past, only moderate functional results and have had a rather heavy mortality. The skilled surgeon, however, may now obtain excellent results by operative reduction, which is advised. Except in experienced hands, the object sought should simply be to improve function by a change in the attitude of the limb by the simplest means or by osteotomy or resection of the head.

The writer describes a modification of the Albee operation which he applies in paralytic dislocated hips (*e.g.*, following infantile paralysis), when the acetabulum is shallow and the hip will not stay in place after reasonable trial by the bloodless method. The operation consists of the turning down of a superior curved lip of bone to overhang the deficient acetabulum and maintain the reduced femoral head. The position of the overhanging lip or rim is maintained by tibial bone grafts inserted between the lip and the bone mass from which it was turned down. The operation includes reefing the capsule, and is followed by plaster fixation for from 3 to 5 months. Sufficient muscle activity may be present to give a good functional hip joint without ankylosis and with excellent stability. E. Jones (Jour. Orthop. Surg., Apr., 1920).

Report of a case of dorsal dislocation of the hip of 13 years' standing treated by a **Lorenz traction apparatus** and later by strong abduction, so that the knee was flat on the table. The head of the femur was thus passed to the front. When the limb was brought toward the midline, the head slipped into its original posterior dislocation position instead of in the acetabulum. The maneuver was therefore repeated and the limb held in abduction in a plaster-of-Paris cast. On palpation the head of the femur appeared to be directly over the acetabulum. Six weeks later an X-ray showed it within the acetabulum. The limb was brought down into slight abduction and a second cast applied. On the removal of the cast at the end of 6 weeks the hip was found to be normal and the patient was able to walk without a limp. J. Shoemaker (Surg., Gynec. and Obstet., xxxii, 461, 1921).

**Dislocations of the Knee.**—These occur rarely and, in order of frequency, forward, backward, outward, inward, and by rotation. The dislocation is frequently compound, and the prognosis rendered much more grave by a complicating injury to either of the popliteal nerves or to the popliteal vessels. Even if, after reduction, pulsation reappears in the arteries of the foot, gangrene may supervene from thrombosis caused by laceration of the inner coats of the artery.

Outward dislocation of the knee is a very uncommon injury. Reduction under anesthetic is accomplished by complete flexion of the knee and hip, the left hand of the operator behind the tibia, with the thumb on the external margin of the patella; the right hand is at the ankle. The lower leg is now internally rotated, traction being made on the tibia and the leg extended. The patella is next slipped into place.

Extension is made for 4 days, followed by immobilization in plaster.

Massage is given after the first week. A perfect result was obtained in a personal case in 6 weeks. Ferguson (Jour. Amer. Med. Assoc., lxx, 1213, 1918).

Forward dislocation may be complete, or, more commonly, incomplete. When complete, the tibia may be displaced some distance upward over the front of the condyles. If the dislocation is compound, the wound is posterior and transverse. The cause is direct violence or hyperextension of the knee. Reduction is easily made by traction and pressure.

Backward dislocations may be complete or incomplete. The leg is usually either extended or hyperextended, and may be deviated to one side. The patella may be dislocated outward. The usual cause is direct violence. Reduction is effected by traction and pressure. Even without reduction a fairly useful limb has resulted in several cases.

Lateral dislocations are outward or inward, complete or incomplete. The patella is usually deviated toward the side of the dislocation. The incomplete form is usually caused by abduction or (inward) by adduction. Reduction by traction and pressure. Dislocation by rotation is said to be incomplete when one condyle revolves around the other, complete when both revolve around a central axis. There may be additional backward or outward displacement. Rotation is outward or inward according to the direction in which the toes turn. Reduction is easy. Knee dislocations should be kept immobilized several weeks.

In habitual dislocations of the knee, the lower end of the femur and upper end of tibia may be drilled and an artificial anterior coronary ligament made of transplanted tendon inserted.

Analysis by the writer of the 21 published specimens of congenital hyperextension shows the pathological lesion to consist in a subluxation of the tibia forward and upward on the femur.

Treatment should be begun at birth and consist at first in manipulation, with narcosis and apparatus if necessary, to reduce the subluxation. In case repeated attempts are unsuccessful, open operation is indicated. Mayer (*Amer. Jour. of Orthop. Surg.*, Feb., 1913).

**Dislocation of the Semilunar Cartilages.**—Either cartilage may be detached from any of its ligamentous

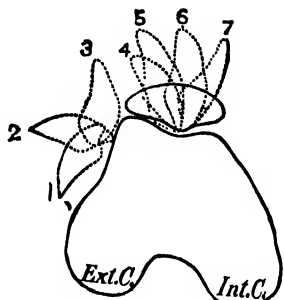


Fig. 16.—Diagram of the various dislocations of the patella. (Stimson.)

attachments, and so displaced in any direction, or it may be lacerated.

The symptoms are those of any loose body in the joint, sudden painful locking, usually after some given movement. The displacement may be recognized by palpation along the articular edge of the tibia. The cause of displacement is a dislocation, a sprain, excessive rotation or flexion.

**Treatment.**—The locking may be relieved by forcible manipulation or by pressure upon the displaced cartilage. Various braces have been devised to prevent recurrence, either by opposing the displacement directly or by preventing the motion which occasions the displacement. These

methods failing, the cartilage should be removed through a short oblique incision alongside of the ligamentum patellæ, with the knee flexed. With careful technique the functional results of this operation are excellent.

Dislocation of internal semilunar cartilage of the knee occurs most commonly when an individual, while standing solidly on one foot, *e.g.*, on a step-ladder or chair, makes a quick move or executes inward rotation at the knee. The internal condyle of the femur, pressing against the cartilage, displaces it inward, rupturing the coronary ligament. In treating this accident, the writer fits a piece of sole leather about 4 inches long and  $1\frac{3}{4}$  inches wide to the inner side of the knee. By first soaking the leather in water and whittling the edges so that it is smooth, it may be molded into shape. It is fastened over the cartilage by adhesive straps—two up and down, one horizontally and one oblique—and covered with a fairly firm bandage. The patients may walk as usual, though for the first three or four days they complain of some local soreness. The bandage is removed and renewed every ten days.

After about 3 such treatments, the patients are well and only a bandage need be used. The irritation of the leather probably causes an aseptic adhesive inflammation to be set up between the loosened cartilage and bone, this taking the place of the ruptured coronary ligaments. G. Chandler (*Jour. Amer. Med. Assoc.*, Oct. 28, 1911).

Report of 10 cases of injury of the semilunar cartilages, comprising 5 fractures and 5 displacements, all of the internal cartilage. Partial extirpation was done in 7 cases, complete extirpation in 2 cases, and suturing in 1 case. The last gave the poorest results. While the best treatment is **extirpation**, in a few early cases cure or improvement can be obtained by **immobilization** for a number of weeks or months with plaster casts



and rest in bed. Reduction should always be attempted by flexing the knee, and, in case of loose internal cartilage, rotating the tibia outward while pressing over the cartilage and then quickly rotating the leg inward with a sudden extension. Where there is posterior displacement, fracture, or a dislocation deep in the joint, complete extirpation alone can cure. Griebenow (*Journal-Lancet*, Apr. 1, 1917).

**Dislocations of the Patella.**—The patella may be dislocated outward or inward, or rotated around its long axis, or the two forms may be combined. Displacement upward or downward is purely secondary to rupture of the ligamentum patellæ or the quadriceps tendon, and need not be here considered.

Outward dislocation is complete or incomplete, and accompanied by various degrees of rotation (Fig. 16; 1, 2, and 3). The patella is readily felt in its new position, though it may be difficult to determine whether the outer or the inner border is directed forward. Muscular action and direct violence are the causes of the dislocation, and hydrarthrosis and ligamentous weakness are predisposing causes. The fibrous expansion of the vastus internus is ruptured, and the muscle itself may be more or less torn. Reduction is made by direct pressure during extension of the knee and flexion of the hip.

Incomplete dislocations are those in which, during extension or flexion, the patella moves outward on to the external condyle.

**Outward, Edgewise, or Vertical Dislocations (by Rotation).**—In these the patella is moved outward and its inner edge backward into the intercondylar groove; so that its articular surface looks outward and more or less forward, or completely forward (Fig. 16:

4 to 7). The causes and treatments are the same as for outward dislocations.

Inward dislocations present the same features, *mutatis mutandis*, as the outward, but they are much less frequent.

Habitual dislocations are usually the result of some deformity, such as genu valgum. They are controlled by correcting the original deformity, or by apparatus, or by tightening up the loose lateral ligaments (by operation).

Wrede observed a family in which bilateral luxation of the patella occurred in the grandfather, father, sister and 1 of his 5 brothers, and his son and daughter.

EDITORS.

The writer applies the **bone graft wedge** treatment in habitual dislocation of the patella. A semilunar incision is made outside the patella, and the external condyle incised for  $1\frac{1}{2}$  to 2 inches, which allows the anterior surface of the condyle to be raised by producing a green stick fracture. Into the wedge-shaped gap thus formed a section of bone from the crest of the tibia is fitted and anchored by dowel pins also made from the tibia. The further displacement of the patella is blocked by the elevation of the external condyle. Albee (*Med. Rec.*, Aug. 14, 1915).

**Dislocation of the Fibula.**—The upper end may be dislocated outward and forward, or backward, or upward. These dislocations are all rare. The first form seems to be caused by muscular action of the long extensors of the foot; the second (in more than half the cases) by action of the biceps, and the third by an injury resembling Pott's fracture, in which the fibula, instead of being broken, is forced upward.

A complicating fracture of the tibia may exist. Recurrence is likely, although reposition is easy, and, hence, immobilization should be maintained for several weeks.

The lower end may be dislocated

backward. This is quite as rare as the dislocation outward in connection with Pott's fracture is common.

**Dislocation of the Ankle (Tibiotalarsal).—Backward.**—By extreme plantar flexion the lateral ligaments are torn, the foot slips back, and the astragalus is caught behind the tibia. (Incomplete dislocation is a frequent accompaniment of Pott's fracture.) The malleoli may be fractured. The lengthening of the heel and shortening of the foot may only be determined sometimes by careful measurement.

**Forward.**—Rare. Caused by pressure on the heel or by exaggerated dorsal flexion.

**Inward.**—Two varieties. In the one the astragalus is pried out by supination and adduction, and the foot moved directly inward and forward; in the other (thought to be secondary to a backward dislocation) the foot is turned over so that its plantar surface faces directly inward. Reduction is easy.

**Outward.**—Appears always to be associated with Pott's fracture.

**Subastragaloid Dislocations.**—The other bones of the foot may be dislocated from the astragalus outward, inward and backward, forward, or backward. The first two are the most common. About 50 per cent. are compound. About 50 per cent. of attempted reductions have succeeded. Complicating fractures are not infrequent. Notwithstanding the persistence of the displacement, a good functional result may be obtained in some unreduced cases. Primary and secondary excision of the astragalus have given good functional results.

**Dislocations of the Astragalus.**—The varieties are forward, backward, outward and forward, inward and forward, and by rotation. There is fre-

quently more or less rotation in connection with the other displacements.

**Outward and Forward.**—This is the most frequent form. The foot is adducted and inverted and the external malleolus prominent. The astragalus rests on the outer cuneiform and cuboid bones, or even on the fifth metatarsal. Its posterior part is still in contact with the articular surface of the tibia. Reduction by traction on the foot and pressure on the astragalus is usually easy, unless the bone is rotated.

**Inward and Forward.**—The foot is abducted and everted, and the astragalus lies in front or below the malleolus. Reduction may be prevented if the tendon of the tibialis anticus embraces the neck of the dislocated bone.

**Forward.**—Very rare. The cases reported have no features in common.

**Backward.**—There may be lateral displacement. In about 50 per cent. of cases the bone was broken at the neck and only the posterior fragment dislocated. There may be flexion of the terminal phalanx of the great toe. Reduction was effected in one-third of the simple cases.

**Rotatory.**—Dislocation by rotation alone may take place about the vertical or transverse axis (in these latter there is always some displacement forward and inward) or about the anteroposterior axis.

Subastragaloid dislocation of the foot, in which the os calcis and scaphoid are displaced from the astragalus, was observed by the writer in 3 cases, 2 of long standing. In each case there had been a violent wrenching of the foot outward by a force applied from above. In a case of 2 weeks' standing **closed reduction** under ether proved satisfactory. For long standing cases he recommends total **astragalectomy**. B. H. Moore (Surg., Gynec. and Obstet., Dec., 1922).

In all severe dislocations of the astragalus the blood supply of the bone is interrupted, perhaps temporarily destroyed. There is no main nutrient artery to this bone. It is supplied by numerous small blood vessels. The bone may be replaced in normal position, however, and a good functioning foot results. Sneed (Jour. Bone and Joint Surg., Apr., 1925).

Removal of the astragalus may be expected to give a good functional result. In flail ankle arthrodesis is valuable.

**Dislocations of the Tarsus and Metatarsus.**—These are too rare and irregular for systematic description.

The writer found 15 cases on record of dislocation of Lisfranc's joint since Lenormant's compilation of 96 cases in 1908, thus aggregating, with 2 personal ones, 113 cases. The luxation was total in 58. Reduction by manual pressure succeeded in only 35 per cent., but the patient got along well with the uncorrected total dislocation, while the outcome was most disappointing in the operative cases. Operation is justified when only a single bone is dislocated. Gruner (Deut. Zeit. f. Chir., Oct., 1910).

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New York,  
AND  
W. WAYNE BABCOCK,  
Philadelphia.

**DIURETIN**, or **theobromine sodio-salicylate**, is a double salt of theobromine-sodium and sodium salicylate [ $C_7H_7N_4O_2Na + C_6H_4(OH)COONa$ ]. Its chief constituent, theobromine, of which it contains about 50 per cent., is a dimethylxanthine, and is therefore closely allied to caffeine, which is trimethylxanthine. It occurs as a white, odorless powder, having a saline and somewhat alkaline taste, and has the advantage over pure theobromine of being soluble in water. Diuretin is hygroscopic and is decomposed when exposed to carbon dioxide or to acids; it should therefore be kept in well-closed containers. It is incompatible with chloral hydrate, phosphates, bicarbonates,

ferric salts, and even traces of free acids. It is official as *Theobromina sodio-salicylas*.

**PREPARATIONS AND DOSE.**—For diuretic purposes, the drug may be given in doses of 15 grains (1 Gm.) as often as five or even six times a day, in adults. In arteriosclerosis smaller doses should be employed: 8 grains (0.5 Gm.) two to four times daily. It may be given in water, but some simple flavoring agent, together with administration of the drug in syrup (not syrup of orange-peel or lemon, however) may be of advantage in that the slight alkaline taste will be disguised. It may also be given in milk. It should be taken between meals.

**PHYSIOLOGICAL ACTION.**—The drug is a powerful diuretic, acting especially by stimulation of the peripheral vasodilator nervous mechanism in the kidneys which results in increased caliber of the renal vessels and a markedly increased flow of blood through the organs. Although it is possible that theobromine acts in part by directly exciting the renal secreting cells, modern pharmacological work has lent no support to such an action, and the statement seems warranted, both from this work and clinical experience, that the drug causes little or no irritation in the kidneys. Gruenwald deems it probable that the glomeruli are chiefly influenced, although paralysis of reabsorption in the kidneys—in regard to salts especially—also forms part of its action.

The writers were able to confirm the strong diuretic action of theobromine in healthy subjects, and a moderate influence in renal disease. Theobromine-sodium salicylate (*diuretin*) gives a weak diuresis, and only in patients with anacidity of the stomach. In retention of water of hepatic origin the preparations of the purin group had no effect. Grossman and Sandor (Wiener klin. Woch., Apr. 9, 1925).

According to Hoffmann, Pawinski, and others, the diuretic effect in dropsy shows itself slightly in the first twenty-four hours after the initial dose of the drug. It becomes well marked after two days, and reaches its height in four or five days, when 5 or 6 liters of urine a day may be voided. Theobromine preparations are superior to caffeine as diuretics in that the action is more pronounced and prolonged and is unaccompanied by symptoms of central nervous excitation.

It is by many considered superior to theophylline (theocin) in causing less gastrointestinal and nervous disturbance, and is certainly, in the average case, likely to cause a more prolonged diuretic effect; sometimes, however, theophylline will induce a more marked and prompt diuresis than theobromine.

In common with the other drugs of the caffeine group, diuretin causes an increase in the elimination of certain salts, especially sodium chloride and the phosphates. The nitrogenous constituents of the urine may also be increased, though to a less extent.

Upon the heart theobromine compounds exert the same stimulant action as caffeine. Upon the vascular system, however, they act differently, tending to dilate the peripheral vessels, as well as the coronaries and renal vessels. The blood-pressure does not fall, but may instead be slightly raised, owing to the augmented heart action (Haynes). The stimulant action of caffeine on the vasomotor center is wanting with theobromine; this is believed to account for the ease with which it maintains the kidneys in a state of increased secretory activity, no constrictor impulses reaching the renal vessels from the vasomotor center no matter what the dose of theobromine given.

Theobromine appears to possess to a certain extent, in common with caffeine, the property of dilating the walls of the bronchioles when these are in a state of constriction, as in the acute asthmatic paroxysm. It slightly increases general muscular power. Rost found in the dog that from 10 to 30 per cent. of the large doses given could be recovered in the urine. A part of the theobromine ingested by any mammal appears to be demethylated to monomethylxanthine before excretion. According to Aubel, theobromine may be found in the urine of man six hours after a dose of diuretin has been ingested, and after twenty-four hours it has completely disappeared.

**UNTOWARD EFFECTS.**—Although it has been reported that in some patients as much as 150 grains (10 Gm.) of diuretin can be given without any untoward result, such large doses will not infrequently induce headache, nausea and vomiting.

Diarrhea is the most frequent unpleasant accompaniment of the more moderate doses, up to 90 grains (6 Gm.) in the twenty-four hours. Other effects which have been witnessed are vertigo and tinnitus aurium, and in occasional cases evidences of central nervous excitation, such as restlessness, insomnia, tremor, and a peculiar feeling of fear. Most adults, however, bear 75 grains (5 Gm.) in a day well, and Hoffmann even found that debilitated patients could usually take up to 105 grains (7 Gm.) without disturbance. Krehl states, however, that after such large amounts a collapse-like condition has been observed, and advises that 75 grains be not exceeded in twenty-four hours.

Pawinski refers to the fact that diuretin may cause headache and tinnitus aurium "like after salicylic acid preparations." It is not unreasonable to suppose that, with the large doses often given, these symptoms are actually due to the salicylic constituent of diuretin. Where they are so marked as to interfere with the use of the drug, the substitution for diuretin of theobromine sodioacetate (see Agurin) would seem advisable.

In animals Schroeder found the fatal dose of theobromine to be five or six times higher than with caffeine. Frankly toxic doses of diuretin are said to produce vomiting, diarrhea, free salivation, dyspnea, elevation of temperature, cardiac acceleration, and diminished arterial pressure.

**THERAPEUTICS.**—Theobromine sodio-salicylate is useful particularly in **dropsy** due to cardiac or renal conditions. In nephritis most clinicians recognize that it can be employed without danger of irritating the kidneys. Among cases of renal disease the best results are seen in **acute nephritis**. Advanced **chronic nephritis** is not infrequently refractory to its action, though Klemperer states that in cases of moderate severity daily doses of 60 to 90 grains (4 to 6 Gm.) will increase the amount of urine 1 to 2 liters. In **parenchymatous forms of nephritis**, a number of observers credit the drug with the property of diminishing the albuminuria, at least temporarily. In the initial stages of **uremia**, good results from it have been reported.

In **cardiac disease** diuretin is useful for several purposes. It is not only helpful as a diuretic in **valvular disease** with edema, in which condition it may frequently be combined with digitalis with advantage, but is sometimes useful as a substitute for drugs of the digitalis group when these prove ineffective in pronounced **chronic myocarditis**, the theobromine in it in this case exerting an action similar to that of caffeine—though less pronounced and constant, according to Sonnenkallb. The heart beats are strengthened and sometimes slowed.

A patient advanced in years, suffering from arteriosclerosis and diabetes, had survived more than a hundred attacks of severe **pulmonary edema**. Fifteen grains (1 Gm.) of diuretin, given during an attack, always improved the heart action. Rosenfeld (Allgem. med. Zentralzeit., No. 18, 1909).

Theobromine is believed to dilate the coronary vessels—unless so sclerosed as to be rigid—much more than caffeine. This doubtless accounts for the excellent results reported from its use in moderate doses in **angina pectoris**. According to Pauli and Kaufmann, it sometimes acts so promptly in this condition that the attacks are checked almost at once. In some instances the patient remains free from the paroxysms when the drug, after a period of continuous use, is left off; in other cases it must be given again after a short period of rest.

The following combination of the drug with sodium iodide may be administered in anginal states:—

*R. Theobrominae sodio-salicylatis* ..... f3j (4 Gm.).  
*Sodii iodidi* ..... gr. viij (0.5 Gm.).  
*Aque menthae pip-erita*,  
*Aque destillata* aa f3iij (90 c.c.).

M. Sig.: To be taken at intervals in one day.

In marked types of angina, viz., those in which the pain is wholly projected to the back, shoulders, arms, lower jaw, etc., the drug has proven of the same utility as in **angina pectoris**. A number of clinicians

have also praised its prompt action in the so-called "**angina abdominis**" or **arterio-sclerotic colic**, ostensibly due to temporary spasm of already partially sclerosed mesenteric vessels. It is considered by Breuer to reduce the abnormal irritability of these blood-channels. According to Burwinkel, the diagnosis of abdominal angina can be made in cases of obscure abdominal pain through the rapid relief afforded by theobromine compounds.

Von Noorden uses it as prophylactic against the **anginal attacks seen with** lesions of the coronary arteries, as well as those met with in **chronic tobacco poisoning** and **neurasthenia**, theobromine is usually more effective than the iodine preparations. Theobromine sodiosalicylate should be given in doses of 7½ to 9 grams (0.5 to 0.6 Gm.) three times a day; larger amounts are unnecessary and are, perhaps, less effective.

In **arteriosclerosis** in general, the drug seems to prove useful in the hands of some observers. It has been especially recommended in the **headache of arteriosclerotics**; here doubtless the salicylate component is sometimes responsible for the results noted. As already intimated, theobromine tends to overcome undue excitability of the vascular tree, thus preventing it from going into spasm or overcoming the spasm where it exists. This would seem to account for the benefit noted by Kaufmann in **intermittent claudication**. It applies both to vascular neuroses without organic lesion and to arteriosclerosis in its earlier stages. Loeb refers to a useful effect of diuretin in cases of arteriosclerosis where the heart gives out owing to increased demands made upon it and because the thickened coronary vessels do not supply it with sufficient blood.

According to Van den Velden and others, theobromine sodiosalicylate will effectually remove the bronchial spasm in cases of **asthma**, relieving the distress entirely or nearly so within fifteen minutes if the drug be ingested at the beginning of the attack. The dose to be used is 15 grains (1 Gm.) in water, which is repeated once, or rarely twice, if there is no relief after ten or fifteen minutes. The drug does not seem to lose its effect, even after daily use for some weeks. S.

**DIVERS' PARALYSIS.** See  
COMPRESSED AIR, DISORDERS DUE TO.

### DIVERTICULITIS, INTESTINAL.

—This condition, though seldom recognized, is relatively common. It consists of hernial protrusions formed of the mucosa of the descending colon or sigmoid flexure (seldom above and ceasing at the rectum) through the thinned muscular layer. The protrusions may be very numerous—several hundred in some cases—and vary in size from that of a millet seed to that of a cherry, often the latter. They often contain fecal masses which assume the density of concretions. All the coats of the intestine may be involved; the diverticula may ulcerate through these, and their contents awaken peritonitis; or the latter may be caused by pathogenic organisms which penetrate the gut. Acute or gangrenous inflammation of a diverticulum with ulceration into the bladder may occur.

[A personal case showed adhesion to the posterior portion of the bladder with considerable thickening of the latter at the area of contact. This area was finally perforated, and fecal matter passed into the bladder, though in small quantities, which were voided by the urethra. A mild cystitis resulted, but this ceased after resection of the sigmoid flexure and closure of the bladder by W. Wayne Babcock, of Philadelphia. Though colon bacilli persisted in the urine some time, recovery ensued. C. E. DE M. S.]

**Symptoms.**—No symptoms may suggest the presence of diverticulitis until perforation occurs, causing peritonitis, left iliac abscess, cystitis, etc. There may be pain of a neuralgic character deep down in the pelvis (as in my case), owing to pressure upon abdominal plexuses or adhesions. Constipation and the passage of repeated small stools, sometimes ribbon-like, often suggest cancer; this is especially apt to be the case when a chronic inflammation of the submucous and serous coats occurs. Any acute catarrhal inflammation may give rise to pain, tenderness, corresponding on the left side to that of appendicitis on the right, and swelling of the left inguinal region, with rigidity of the rectus, fever and leucocytosis.

**Complications.**—As a result of infection through intestinal diverticula, J. W. Keefe (Boston Med. and Surg. Jour., Feb. 22, 1917) enumerates the following grave, and not infrequently fatal, complications: (a) chronic extramucosal inflammation, frequently resulting in tumor formation and simulating carcinoma; (b) peritonitis resulting from the perforation of a diverticulum; (c) abscess formation; (d) intestinal obstruction, due to adhesions of the inflammatory mass to contiguous structures; (e) fistulæ and fistulous tracts, particularly between intestine and urinary bladder; (f) chronic mesenteric; (g) metastatic suppuration in the liver; (h) malignant changes.

**Diagnosis.**—*Appendicitis* sometimes causes confusion, particularly when left sided. *Tuberculous colitis* may be identified sometimes by finding tubercle bacilli, pus and blood in the stools; the tuberculin test is helpful.

In 3 cases of diverticulitis with röntgenologic findings reported by R. D. Carman (Annals of Surg., lxi, 343, 1915) the patients were somewhat obese. The salient symptoms were: abdominal pain, usually severe, often localized in the sigmoid or descending colon; constipation was the rule. Vesical symptoms, as frequency and tenesmus, were occasionally noted. In every case where the sigmoid was involved, a mass could be felt. Proctoscopic examination was positive in one case where a partial intussusception had taken place. Blood was absent from the stools owing to the extramucosal location of the disorder.

The X-ray findings may aid in the following way: the position of the cecum in differentiating it from left-sided appendicitis. Filling defects may be present in the plates in both carcinoma and diverticulitis, but the presence of extraluminal shadows would suggest diverticulitis. Where a carcinoma developed upon a diverticulitis, the characteristic extraluminal shadows would be present, while if the shadows were absent the growth would suggest a carcinoma.

Phleboliths or calcified glands give shadows resembling diverticula filled with bismuth or barium; if situated high in the sigmoid, palpation during a screen exami-

nation may reveal the fact that they do not move with the bowel. Lower down the bowel is not sufficiently movable to make this differentiation. The opaque ingested meal offers less chance than the bismuth enema of detecting diverticula.

**Etiology.**—Diverticulitis occurs more frequently in males than in females and may occur at any age, though most frequently observed during the sixth decade, and occasionally later. Obesity is present in more than one-half of the cases. Prolonged retention of feces, flatulence, constipation, mesenteric congestion, congenital laxity of the connective tissue around the vessels, and muscular deficiency, local or general, of the intestinal wall, leading to dilatation, are frequent causes.

**Treatment.**—This depends upon the character of the lesion. Acute peritonitis, cystitis, or intestinal obstruction demand celiotomy and **resection** of the diseased segment with end-to-end anastomosis, after carefully cleansing out the intestine. When recognized before perforation occurs **high enemas, fluid diet and rest in bed** sometimes cause an acute attack to cease, and further attacks may be warded off by the frequent use of **saline aperients** to keep the stools soft. **High olive oil irrigations** are also of value.

The surgical procedures that are applicable in most cases, according to J. W. Keefe (Boston Med. and Surg., Feb. 22, 1917) are as follows: through a left rectus or muscle splitting incision in the left iliac region, the left lower quadrant is explored, and if an abscess is found it is drained. Although some surgeons advise the removal of the diverticulum coincidentally with the draining of the abscess, deferring this to a later time, when a more extensive operation can be undertaken with less hazard to the patient, is favored by the writer. The two-stage operation often gives good results. A loop of the bowel containing the affected area is drawn through the abdominal wound, and the walls of the normal bowel above and below this mass are stitched together. The two portions of the bowel below the loop of the intestine withdrawn are then sutured to the parietal peritoneum. About 48 hours

later the diseased area of the bowel is removed with a cautery, thus completing a colostomy. A secondary operation may be performed at some future time, and the openings in the bowel closed.

In cases of fistula between the bowel and the urinary bladder, the surgeon should first make a careful cystoscopic examination, to determine the size and location of the opening in the bladder. The peritoneal cavity is then opened, the adherent colon and diverticulum separated from the bladder, and the opening in the latter is now closed. The involved colon may then be resected and end-to-end or a lateral anastomosis made, but here, too, the more conservative two-stage operation should be the choice in many instances. As to the relative advantages of lateral compared with an end-to-end anastomosis, the former, when we have sufficient bowel to work with, is preferable on account of the greater tendency in the latter to leakage at the mesenteric border.

Statistics from various authorities have shown conclusively that extensive resections of intestine, done in the presence of infection, as is always the case in operations for diverticulitis, are, in a large percentage of cases, fatal. S.

## DIVERTICULUM, MECKEL'S

**—Pathology.**—Meckel's diverticulum, which is found in children with a frequency of 1 in 60 or 1 in 100, is very often, as stated by Bienvenu (Thèse de Paris, 1912; Surg., Gynec. and Obstet., Feb., 1913), the cause of early pathological conditions, of which intestinal occlusion is by far the most frequent. This may be produced mechanically (volvulus, invagination, or strangulation) or by inflammation (an old diverticulitis).

Diverticulitis may be plastic or suppurative. In the latter case the general picture of peritonitis may be present, as in appendicitis. There are 2 phases of inflammatory occlusion—the first, pseudo-appendicular; the second, occlusion. Beyond this the symptomatology is not clearly defined.

**Diagnosis.**—Meckel diverticulitis may be assumed, according to Bienvenu (Thèse de Paris, 1912), when perium-

bilical pains are present, when there is marked swelling in the umbilical region, with an associated low temperature and quickened pulse; the abdomen only later becomes slightly rigid and tympanitic. The co-existence of another malformation, in particular a tumor or a fistula of the umbilicus, should be taken into consideration in making a diagnosis.

Disease of Meckel's diverticulum seems to be uncommon, although the organ in some form is found in 1 to 2 per cent. of people. According to J. P. C. Griffith (*Jour. Amer. Med. Assoc.*, May 23, 1914), it may be the seat of the following conditions: Strangulation of the intestine by the diverticulum or its remains; persistence of the diverticulum, with an opening at the umbilicus; formation of a cystic tumor; concretions of varying size in the diverticulum; superinvolution of the diverticulum; stenosis of the ileum by a short diverticulum attached to its distal extremity or elsewhere; invagination of the diverticulum, liable to be followed by an ileocecal intussusception; volvulus of the diverticulum, or of the ileum; hernia of the diverticulum; inflammation of the diverticulum.

The diagnosis of diverticulitis is summarized as follows: 1. Localization of pain and tenderness, not so often at McBurney's point as somewhat higher and to the right of the umbilicus, or even about it, or in some entirely different region. 2. An area of puffiness or of firm resistance in this region. 3. Absence or slight degree of meteorism, at least early in the attack. 4. Blood in stools and vomited matter. 5. Previous existence of an umbilical fistula, or of some malformation elsewhere.

E. Kirmisson (*Bull. de l'Acad. de méd.*, Apr. 25, 1916) draws attention to the possibility of confounding intestinal obstruction due to constriction of Meckel's diverticulum with acute appendicitis.

**Treatment.**—The treatment of intestinal occlusion due to diverticulum varies, as stated by Bienvenu (*Thèse de Paris*, 1912), with the case—simple resection of the diverticulum, resection of intestinal flexures, or the formation of artificial anus. Whenever in the course of any operation the presence of a diverticulum

is discovered, it should in every case be removed. If an operation, following abdominal complaints, should prove the appendix to be in a healthy condition, it will be well to examine the last few centimeters of the ileum for a persistent diverticulum.

In troublesome cases of Meckel's diverticulum open at the umbilicus, forming a fecal fistula, Kirmisson (*Bull. de l'Acad. de méd.*, Apr. 25, 1916) first ligates the pouting margins of the canal to prevent outflow of feces, next incises around the umbilicus through the peritoneum, delivers the diverticulum and loop of intestine to which it is attached, ligates the diverticulum at its base, removes it with the thermocautery, buries the stump, and closes the abdomen. Three cases were thus treated successfully. Infants operated on for this condition should be breast-fed to improve their resistance.

S.

**DOVER'S POWDER.** See OPTIUM.

**DROPSY.** See ASCITES AND EDEMA.

**DROWNING.**—In most cases individuals who have been asphyxiated from submersion in water for over five minutes are dead when they are taken out, but modern research has shown that the vital spark lingers long in the body cells and all efforts to revive the victim should be made, long after the five minutes have elapsed. Cases have been revived after immersion had considerably exceeded the usual limit, some as much as one-half hour.

Two cases of individuals who had been in the water for a time considerably longer than is usually followed by recovery. They tended to show that the best method of artificial respiration without apparatus is that of **Sylvester**, where there is but one operator, and the combined **Sylvester and Howard methods**, as suggested by A. H. Smith, where there are two or more to assist in the work. These are the methods prescribed in the regulations of the Life-saving Service. The first case



had been submerged 23 minutes, and the second nearly *half an hour*, and yet the boy recovered after an hour. Trask (Milit. Surgeon, May, 1907).

The first thing to be done is to promote the expulsion of the water from the respiratory passages. The best way to do this is to hold the patient in the vertical position the head downward. This is especially applicable in the case of children, but sometimes difficult when the patient is an adult. Laying the patient abdomen down over a barrel will sometimes act as a substitute. The next thing to do is to perform artificial respiration, of which there are several methods.

If any considerable quantity of water has entered the bronchial tubes, unless it is very quickly expelled by a voluntary effort, such cases are hopeless. The condition is shown by the continued expulsion of froth when artificial respiration is performed, although the mouth and pharynx have been well wiped out before commencing. Barnes (Lancet, June 18, 1910).

**Artificial Respiration.—Marshall Hall Method.**—The following method was first described by Marshall Hall in 1857: The patient is alternately rolled from the lateral to the prone position, pressure being made on the back between the shoulder-blades while in the prone position. The advantage of this method is that the tongue does not fall back, obstructing the flow of mucus and water from the mouth.

**Sylvester Method.**—Sylvester described another method in 1858, but one disadvantage is that at least three persons are required to perform it. The patient is placed upon his back with a small roll under the neck, the shoulders being slightly raised. The arms of the patient are grasped just above the elbows by the operator, and gently moved away from the body to a point over the head. The ribs are thus raised and the capacity of the chest increased.

The arms are then brought down to the side, the elbows flexed and pressed against the chest. This decreases the capacity of the chest and expels the air from the lungs.

With the exception of the **Brosch-Sylvester method**, the **Schäfer method** of artificial respiration gives the greatest respiratory exchange for each thoracic movement. In addition to this, there is free drainage for the lungs. Hitchings (Jour. Amer. Med. Assoc., Nov. 23, 1912).

**Howard Method.**—Still another method was described by B. Howard, of New York, in 1868. The operator kneels over the patient and exerts pressure on the lower part of the chest, diminishing the chest capacity. The pressure is then relieved, thus increasing the chest capacity. But in this method the tongue tends to fall back into the pharynx; the ribs may be fractured, especially in senile subjects, when they are quite brittle, and the liver is liable to be ruptured, as it is enlarged and congested in such cases.

**Schäfer Method.**—The "prone pressure" method seems to be the best so far introduced. It was first described in 1890 by E. A. Schafer, of Edinburgh.

In cases of drowning the prone pressure method of artificial respiration is always indicated. Its advantages are: (1) that it is fully efficient; (2) that it can be performed without fatigue by a single individual; (3) that it is simple and easily learned, and (4) that it allows the tongue to fall forward and the mucus and water to escape from the mouth, so that the tendency of these to block the passage of air, which is inherent to the supine position, is altogether obviated. It can be applied equally well in attempting to revive a patient whose respiration has ceased in consequence of an overdose of chloroform or other anesthetic. Schafer (Jour. Amer. Med. Assoc., Sept. 5, 1908).

The prone pressure or Schäfer method of resuscitation is preferable to any of the other manual methods. Third Resuscitation Commission (Surg., Gynec. and Obstet., Jan., 1919).

The patient is placed in the prone position, vertical pressure being applied over the ribs, the operator kneeling beside the

patient. This causes the thorax and abdomen to be compressed against the ground, the pressure on the latter forcing the viscera upward against the diaphragm, which moves upward, forcing the air from the lungs. The pressure is then relaxed and the parts return to their normal position, thus drawing the air into the lungs. This procedure is performed about twelve times a minute.

The patient should be **kept** as **warm** as possible, woolen blankets being wrapped

sult of a number of afferent impulses partially paralyzing the vasomotor center, and so causing a rapid fall in blood-pressure; the result of this is that the greater portion of the blood of the body stagnates in the splanchnic area, and the brain, including the circulatory and respiratory centers, is robbed of its proper supply, and these centers are still further depressed. The result to be aimed at, therefore, is the driving of the blood



Fig. 3.—Stimulating respiration by slapping and massage.

around him after he has been thoroughly dried. During the artificial respiration **gentle friction** should be made always toward the center of the body. Artificial respiration should be continued as long as the heart continues to beat, and it is said the movements should be continued for from one to two hours after the heart has ceased to beat.

The usual directions given for the treatment of the apparently drowned are to perform artificial respiration and apply warmth. If, however, we look upon such as cases chiefly of shock, it is obvious that something more than this may be done. Shock may be looked upon as the re-

sult of a number of afferent impulses partially paralyzing the vasomotor center, and so causing a rapid fall in blood-pressure; the result of this is that the greater portion of the blood of the body stagnates in the splanchnic area, and the brain, including the circulatory and respiratory centers, is robbed of its proper supply, and these centers are still further depressed. The result to be aimed at, therefore, is the driving of the blood

from the abdomen, so that the brain may receive its proper supply. This may be done by an attempt at **auto-transfusion** as follows: Having started an assistant on artificial respiration, the author firmly bandages the legs from the feet upward. A roller towel is then passed round the patient's abdomen, the two ends crossing in front. One assistant is told off to each of these ends. As the arms are brought down to the chest in the *expiratory* movement of artificial expiration (Silvester's method) these two assistants, grasping the towel ends firmly with their right hands, pull them, at the same

time making pressure on the abdomen with their left hands. In this way considerable squeezing of the abdomen is obtained. As the *inspiratory* movement commences the pressure is relaxed so as not to interfere with the expansion of the lungs. The process is continued synchronously with the movements of artificial respiration. The idea is that this acts beneficially in two ways: (1) it assists, by pressing on the diaphragm,

seems hardly to apply in cases of drowning, as when once reaction has set in recovery is usually rapid. **Adrenalin chloride** given hypodermically (30 minims—1.8 c.c. of a 1:1000 solution) should act beneficially by raising the blood-pressure. Barnes (*Lancet*, June 18, 1910).

The patient, reviving, should be removed to a warm room and kept quiet, and later such stimulation and tonics should be given as is deemed necessary.



Fig. 4.—Expelling water from lungs and stomach.

to more completely empty the chest with expiration; (2) it squeezes some of the excess of blood from the abdominal cavity. The bandaging of the legs and arrangement of the towel can be very quickly carried out with assistance, of which there is usually no lack in these cases. Gravity should also be made to assist the flow of blood to the brain by keeping the head at a lower level than the body. The writer gives a hypodermic injection of **ether** (30 minims—1.8 c.c.) and usually one of **strychnine** as well. The objection to the use of these stimulants—that they stimulate an already tired center and are quickly followed by increased depression—

In some cases of drowning attributed to cardiac failure the swimmer simply loses consciousness from cerebral anemia—*i.e.*, he faints, goes under, and inevitably perishes unless help is at hand. Apart from disease, such as aortic disease or cardiac dilatation, several other causes may bring about such a state of things. Among them are severe and prolonged muscular effort prior to swimming, and flatulent dyspepsia. Every person in the habit of swimming in deep water should have a medical examination from time to time. To enter the water with a full stomach is probably as dangerous as with an empty one. About two hours

after breakfast or lunch is the best time. When the intestines have been emptied by a purgative and the circulation depleted thereby, swimming in cold water should be avoided. Lawrie (Brit. Med. Jour., Sept. 16, 1905).

The following details on the prevention of drowning, rescuing, and the treatment of the apparently drowned, published in the Pennsylvania Health Bulletin of May 12, 1912, under the auspices of Dr. Samuel

kept up for a long time without tiring. If unable to keep the head above the surface constantly, every time it goes under the mouth should be closed and the breath held, thus preventing strangulation.

"Prevention of chilling the body is of the greatest importance, and if there is long-continued exposure in the water as in the case of ship-wrecks, it is advisable to put on an abundance of woolen clothing, if at all possible.

"In salt water when the current sets out

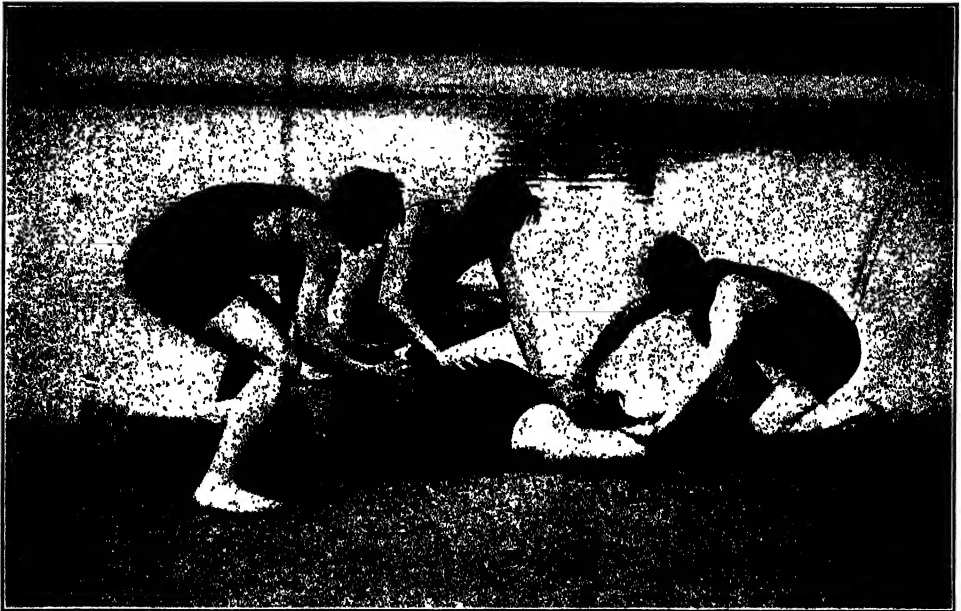


Fig. 5.—Inducing inspiration (more than one operator). Tongue held by handkerchief.

G. Dixon, the Commissioner of Health, are so helpful that we take the liberty of presenting them practically *in toto*:—

**"Prevention.**—When in danger of being drowned the individual should remember that in order to keep afloat the hands and arms should be kept under the water and in motion; when they are held out of the water, the head is almost immediately submerged. It is not at all difficult to keep afloat, if this rule is followed, as the human body is of nearly the same specific gravity as water. If one can keep his presence of mind a very slight up and down motion of the hands and feet, paddling as a dog swims, will be sufficient to keep the head above water, and can be

from land, as when the tide is going out, it is a mistake to struggle to reach the land. One should throw himself upon his back, whether alone or encumbered, and await help from the shore. Many persons perish by exhausting themselves in vain attempts at swimming, especially against the current, when it would have been safe to float with the face up, and to wait until rescued.

**"Rescuing.**—If there is no one present who can swim when an individual is drowning, a plank or any piece of wood or rope should be thrown to him to which to cling, urging him to keep his hands under water and to keep both hands and feet in motion.

"Before swimming to the rescue of a drowning person, one should relieve himself of as much clothing as can be quickly thrown off. Be sure to loosen the legs of drawers if they are tied at the ankle. If this is not done, the garment is likely to fill and to act as a drag.

"Do not touch the drowning person so long as he still struggles. Wait until he becomes quiet, otherwise he may grapple with you and render you helpless. As you approach the drowning person, assure him

person who is being saved, above water. By maintaining the position described—the rescuer on his back and the rescued lying face up on the rescuer's stomach—one also will find that it is possible to float for quite a long time.

"If the person sinks before being reached, watch for the bubbles rising from the lungs, which will often enable you to locate the body. In flowing water allowance must be made for the direction and rapidity of the current, as it will carry

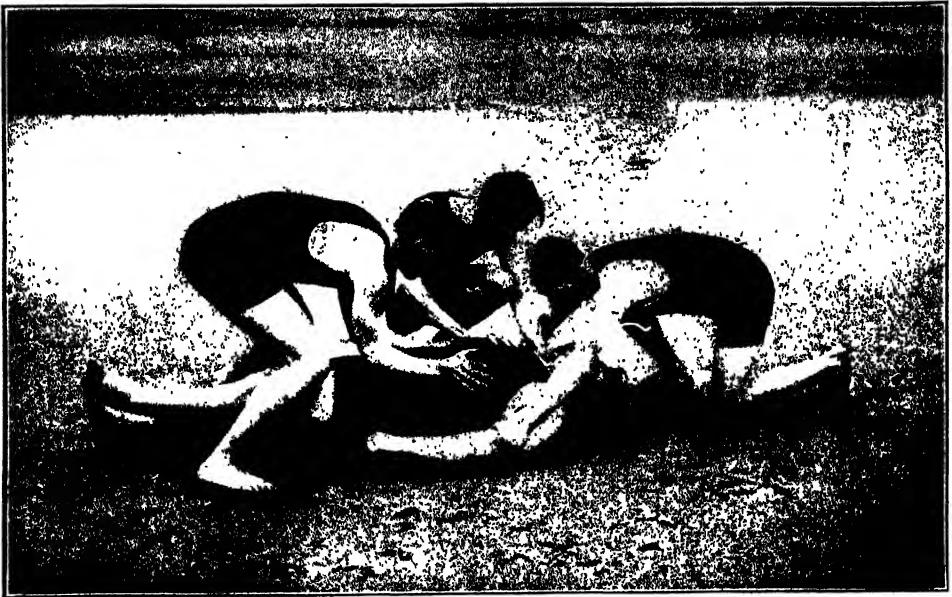


Fig. 6.—Inducing expiration (more than one operator).

in a firm voice that he is in no danger if he will keep quiet. Catch him quickly by the hair or collar, or under the arms, turn him on his back and give him a quick pull. (Fig. 1.)

"This last movement will bring him well up on the surface of the water for a moment. Now quickly throw yourself on your back and haul his back up to cover your stomach; the back of his head will then be on your chest; with both hands holding him, one placed on each side of the lower jaw, swim for your destination. (Fig. 2.)

"If one is a good swimmer he will get to safety in this way sooner than any other. Moreover, one will be able to keep his own face, as well as the face of the

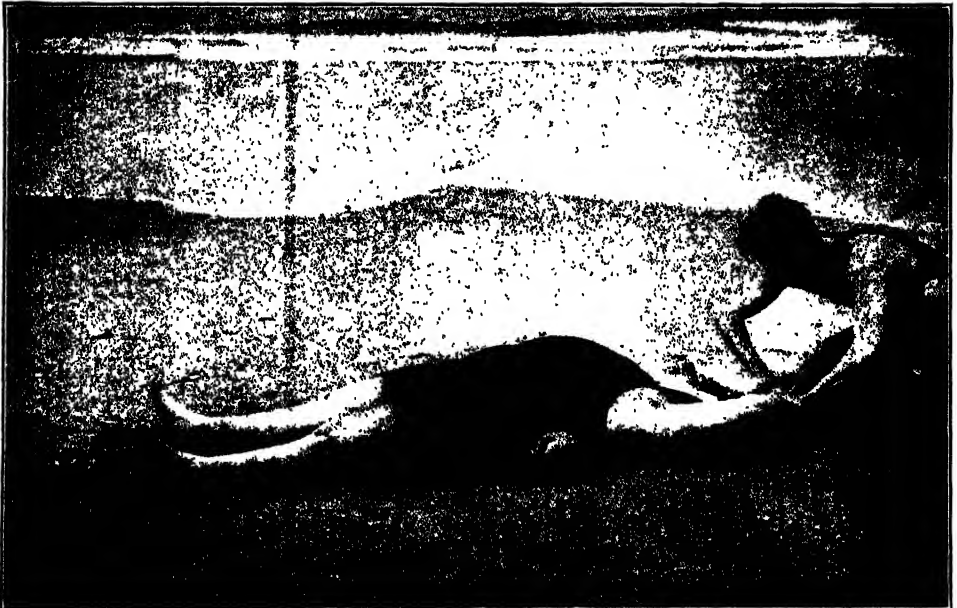
the bubbles down stream from the body. In diving after a body you should seize it with one hand only, leaving the other free to be used in rising to the surface.

**"First Treatment of the Apparently Drowned.**—The first impulse in discovering the body of a drowned person is to summon a physician. Unfortunately, however, under circumstances attending this accident the physician is so infrequently present or within reach that the most valuable time is lost in searching for one. Upon discovering a body every effort should be made at once to resuscitate the victim. It is of the utmost importance that everyone should understand the few simple measures necessary to retain life; and, as it may be necessary to maintain

efforts for a long time, it is important that all methods should involve as slight an outlay of the rescuer's strength as possible. In each instance the aim should be to restore breathing. If the heart has ceased to beat the person is probably dead, but the time required to determine whether this is the case may be fatal. Efforts to restore respiration should be begun at once. Very efficient methods for the restoration of respiration by various mechanical devices are in use by large

mouth free from the ground, keeping the face turned down and heading to the wind, as you want all the movement of air possible. Place a roll of blanket or clothing under the upper portion of the abdomen just below the tip of the breast-bone, as shown in *Figure 3*. Turn his body on its side for a moment and slap the bared chest smartly two or three times with the open hand and let him fall into his former position. (*Fig. 3*.)

"If the patient does not immediately



**Fig. 7.—Inducing inspiration (one operator). Tongue held between the teeth.**

industrial corporations and by many institutions, and are of service when one is apparently dead from electrical shock or from inhalations of water, gas, smoke, or poisonous vapors. The following method, if carefully carried out, will give maximum results:—

**"Rule I. Preliminary Treatment.**—Do not move the patient far from the scene of accident unless he is in danger of freezing. Do your best to keep people from crowding around and shutting off the air. Wipe dry the mouth and nostrils, quickly open the clothing sufficiently to expose the chest and waist. Turn him upon his face, placing one forearm or some other prop under the forehead to keep the nose and

begin to revive, proceed according to Rule II.

**"Rule II. To Expel Water from the Body**—Separate the jaws and keep them apart by inserting something hard between the teeth—a piece of wood, rock, or cork, anything to keep the mouth open. (*Fig. 4*.)

"Take position astride the patient's hips with your elbows resting upon your own knees, and your hands over the body ready for action. Make pressure on the base of the chest until the flow of water from the lungs is slackened. Relax and again make pressure, alternating relaxation and pressure until the lungs are empty. This procedure should not last

longer than thirty or forty seconds and permits the entrance of sufficient air to stimulate respiration.

**"Rule III. To Produce Breathing.**—Clear the mouth and throat of mucus by means of a handkerchief, piece of garment or any rag wrapped around the forefinger. If ammonia, bay-rum, or ether is at hand, use the fumes to stimulate respiration by holding the bottle in front of the nose. Turn the patient upon his back with the roll so placed under him as to elevate the

changing hands if necessary, so as not to interfere with this movement. Just before the patient's arms reach the position last described, the man standing over the body will grasp it with both hands, letting the balls (base) of the thumbs rest on either side of the pit of the stomach, and allowing the fingers to fall into the depressions between the short ribs. Now using his knees as a pivot he will, at the moment the patient's hands touch the ground, throw (but not too suddenly) all



Fig. 8.—Inducing expiration (one operator).

stomach above the rest of the body. Let an assistant, using a handkerchief, draw the tongue out at the corner of the mouth and keep it projecting between the lips (this prevents the tongue dropping back and closing the windpipe). Now let another assistant, placing himself above the patient's head, grasp the patient's arms just below the elbows and draw them steadily upward and over until they extend past the head, parallel with the ground, the hands meeting, as in *Figure 5*.

"(This movement expands the chest and induces inspiration.) The person at the head now moves the patient's arms down beside the body as in *Figure 6*.

"The assistant who holds the tongue,

his weight forward on his hands and at the same time squeeze the waist, increasing the pressure while he slowly *counts four*, and after a final push lets go. (A child or a delicate person should of course be handled more gently.) At the instant the pressure on the chest is released, the operator at the patient's head will again draw the arms upward and hold them extended beside the head while the *count of four* is repeated. This manipulation of the arms and chest is called the bellows movement. It should be kept up deliberately and perseveringly.

"If natural breathing be not restored within, say, four minutes it may be because the air-passages are obstructed by mucus

or water. In any event turn the patient again upon his chest and do as directed in Rule II, rolling the body over in the opposite direction from that in which it was turned when the rule was first followed. After repeating the directions of the rule turn the patient once more upon his back and continue artificial respiration for from one to four hours, or until breathing is established or a physician has declared him dead.

"While care should be taken not to in-

"With rolled blanket or clothing under his back, take position above the patient's head; grasp arms near the wrists and draw them steadily upward and forward (movement to induce inspiration) as instructed in Rule III. Next lower them (here the operation differs from that employed when two persons are working the bellows movement) to the patient's sides, bend them and bring them toward each other until the hands meet over the lower ribs, then press downward and inward



Fig. 9.—Inducing Inspiration by relaxation of pressure.

terfere with the action of those working the bellows movement, the limbs of the patient should be rubbed from the very beginning if a sufficient number of persons are at hand. The rubbing should be done *always toward* the body with a firm grasping pressure, using the bare hands, dry flannels, or handkerchiefs. If possible, warmth of the body should be promoted by the application of heated flannels to the stomach, and hot-water bags or heated bricks or stones to the limbs and soles of the feet.

**"When No Assistants are at Hand.**—If one person must work alone, first, do as directed in Rules I and II, then place the patient face up, as in *Figure 7*.

with a firm, steady pushing movement, as in *Figure 8*.

"Repeat these movements while counting as directed in Rule III. If the jaws be separated the teeth may be made to hold the tongue at the corner of the mouth by passing a handkerchief under the chin and tying it over the head.

**"Alternate Method.**—If the patient has been in the water for a long period of time or, if for any reason the work of resuscitation depends upon only one person, the following method can be used and can be kept up for a longer time without great exhaustion.

"The patient is placed on his abdomen in the position shown in *Figure 3*. The



operator kneels across the patient as in *Figure 9*, the hands being placed at the base of the chest over the lowermost ribs in such a way that the extended fingers are about six inches below the armpits. (*Fig. 9.*)

"Now swing your body forward so as to have your weight fall at a slight angle on the wrists; the elbows are braced against the knees so that the weight of the body is augmented by such pressure as may be had by forward pressure of the feet and

breathe, the process of artificial respiration should be stopped. Place the patient on his back and press the base of the chest *every other* time he breathes *out*, as described under Rule III, *Figure 6*. This should be continued until he can breathe naturally (not too rapidly) without assistance. As soon as this is accomplished the measures described as the "After Treatment" should be carried out.

**"Rule IV. After Treatment.**—As soon as breathing is established the patient should



**Fig. 10.**—Producing expiration by direct pressure.

legs; the legs act as the fulcrum. (*Fig. 10.*)

"This makes lateral and slightly upward pressure on the base of the chest and expels the air from the lungs. Swing back, releasing the pressure as shown in *Figure 9*, and the lungs fill by normal expansion.

"Repeat this motion slowly, about 12 times per minute, exerting no more force than is necessary to cause a deep expiration. The latter can be estimated by the sound made by the air escaping from the mouth and nostrils. (Be careful not to make too deep, sudden, or violent pressure, as injury may be done to the organs beneath.)

"When the patient is beginning to

be stripped of all clothing, wrapped in blankets and put to bed comfortably warm, but with plenty of fresh air. Whisky, brandy, or other stimulants, and hot water, should be given in teaspoonful or dessertspoonful doses, at intervals of ten or fifteen minutes during the first hour.

"After reaction is fully established there is danger of congestion of the lungs, and if perfect rest is not maintained for at least forty-eight hours the patient may be seized with great difficulty in breathing. If this happens death is likely to occur unless immediate relief is afforded. In such cases a large mustard plaster should be applied to the chest. Should the pa-

tient begin to gasp before the plaster takes effect, carefully assist respiration by the bellows movement as explained in Rule III."

**Accessory Measures.**—Various accessory measures may be employed to assist resuscitation. Prominent among these is **adrenalin chloride**, 30 drops with saline solution (at 108° F.—42.2° C.) injected intravenously, or into the radial as recommended by Crile. The needle of the saline solution apparatus is the one introduced into the vessel, while the hypodermic syringe containing the adrenalin is plunged into the rubber tube of the apparatus, and the drug allowed to mix with saline solution drop by drop. When this measure cannot, for one reason or another, be carried out, intramuscular injections of 10 to 20 minims (0.6 to 1.2 c.c.) of **adrenalin** may be tried. **Bleeding** is advocated by some others particularly with the above measures carried on simultaneously.

The **Laborde method**, which consists in drawing out the tongue, held with a handkerchief to prevent slipping, rhythmically eighteen times a minute, is very helpful, assisting greatly artificial respiration. **Oxygen**, ready to be inhaled as respiration is resumed, greatly hastens recovery.

The **induced current**, one pole being applied over the phrenic nerve and the other over the sixth costal interspace, on either side, the sponge being moistened in salt water to insure penetration, sometimes causes violent contractions of the diaphragm, which also aids the artificial respiration method carried on simultaneously.

When nothing seems to cause the heart to resume its beats, **pricking of the heart** with a sterilized or carefully washed shawl-pin, through the chest wall, will sometimes suddenly cause it to resume its beats. As a last resort, opening of the abdomen to practise **heart massage** (see page 138 in the third volume) might be tried.

All methods indicated in the treatment of shock (*q.v.*) or asphyxiation by gases are as applicable to the treatment of drowning.

H. AND S.

**DUBINI'S DISEASE.** See CHOREA.

**DUBOISINE** is the poisonous alkaloid of the leaves of *Duboisia myoporoides*, a plant growing in Australia. It crystallizes in fine, colorless needles, and is considered practically identical with hyoscyamine. The drug is not official.

**PREPARATIONS AND DOSE.**—This alkaloid is generally used in the form of duboisine sulphate, the dose being  $\frac{1}{200}$  to  $\frac{1}{60}$  grain (0.0003 to 0.0013 Gm.).

**PHYSIOLOGICAL ACTION.**—Duboisine sulphate is used as a sedative, hypnotic, and mydriatic. It tends to disturb digestion, producing a disagreeable taste in the mouth, excessive dryness of the mucous membranes, and a loss of appetite. In those having an idiosyncrasy it may cause sweating and salivation. It is said to decrease the quantity of urine and to have a deleterious effect upon nutrition. It is rather irregular in its action.

**THERAPEUTICS.**—Duboisine sulphate may be used instead of atropine to produce mydriasis before ophthalmoscopic examinations, the after-effects being less persistent than when atropine is used. It is recommended in the **night-sweats of phthisis** and **vesical tenesmus**. The drug may also be used for its sedative effect in great **mental excitement**. De Montyel found that large doses of duboisine produced vomiting in the insane without any evidence of nausea. In **epilepsy** and **paralysis agitans** the drug is sometimes useful,  $\frac{1}{100}$  grain (0.0006 Gm.) being given three times a day. It may be employed as a hypnotic in **insanity**, and is said to be less dangerous than hyoscyne.

H.

**DUOTAL.** See GUAIACOL CARBONATE.

**DYSENTERY**, or **Bloody Flux**.  
**DEFINITION.**—An intestinal flux of bacillary or amebic origin, occurring sporadically or in endemic or epidemic form. The large bowel (rarely the small intestine also) is the seat of an intense inflammation with ulceration, necrosis or gangrene, characterized clinically by frequent, serous, bloody stools, with more or less mucus, with tormina and tenesmus,

and, in the acute phases, accompanied by fever.

**VARIETIES.**—Two definite types exist, etiologically considered, viz., *bacillary* and *amebic*, though *pseudo* forms may result from dietetic errors, mechanical or chemical irritants or ptomaine poisoning, rarely from parasites. True dysentery differs in its cause, course, severity, type of lesion, complications, mode of transmission, and geographical distribution. It is customary with some authors to speak of dysentery other than amebic, as catarrhal or diphtheritic or, more correctly, diphtherial; but we shall consider it from the etiological standpoint as bacillary and amebic.

Both the bacillary and amebic types of dysentery were moderately prevalent in both the French and English armies. The amebic form occurred during all seasons of the year, while the bacillary form occurred only in hot weather. At some portion of the front the Shiga infection was most important, at others those due to the other strains. A number of persons suffered simultaneously from both infections. Park (Med. Assoc. Greater City of N. Y.; N. Y. Med. Jour., Nov. 2, 1918).

### BACILLARY DYSENTERY.

This may develop in any inhabited region of the globe, increasing in frequency and severity as the subtropical zones are approached. It occurs sporadically or in epidemics or epidemics. Our knowledge concerning the common origin of these various forms, the *Bacillus dysenteriae* varying only in certain minor details, we owe especially to the work of Flexner and his pupils, Vedder and Duval.

Sporadic dysentery speaks for the ubiquitousness of the causative organism as it may arise anywhere and at any season, especially in the senile,

less frequently in children, and particularly in those whose nutritional state for any reason is deprived. Endemic dysentery is a disease of warm climates, where it may be met at any season, though of greater incidence during the periods of greatest heat, and more or less constantly in the tropics, where seasonal variations are less pronounced.

*Epidemic Dysentery.*—At long intervals this has occurred over great areas, arising in scattered foci, often remote from one another, subsiding during the colder periods to reappear with increasing violence during the summer, and perhaps reappearing over a period of several years. Local outbreaks are more common, however; indeed, they are the rule during hot, dry seasons in most of the countries of continental Europe. Epidemics also occur in such institutions as jails or asylums, homes for children or the aged, and in camps or barracks. These may occur at any season, but the two chief factors of collateral import are heat and drought. The hygienic and social status of people are likewise of determining importance. Bacillary dysentery is always endemic in the Philippines.

**SYMPTOMS.**—The incubation period, according to Strong and Musgrave, does not exceed forty-eight hours. The invasion is usually abrupt, occasionally preceded by constipation, usually ushered in with diarrhea, which in some instances does not in itself excite suspicion as to its real character. Fever, abdominal pain, and frequent stools are usually the first symptoms, with loss of appetite and malaise. At first mucous stools; then bloody, even pure blood, with distressing tormina

and tenesmus, the pain being most intense about the umbilicus and radiating over the outer confines of the abdomen especially, accompanied by nausea, sweating, and more or less collapse. Any food or drink at once excites peristalsis. The desire to evacuate, at first temporarily relieved by a movement, becomes constant and increased by the act. In consequence of frequent, irritating stools, the anal region and rectum become intensely inflamed, at first with increased sphincter contraction, then relaxation and, still later, rectal prolapse. As in any case of severe diarrhea, there is a tendency toward vesical tenesmus also, probably due to the close autonomicocerebrospinal association of bowel and bladder. Frequent, burning micturition results. During the early stages, within the first few hours in fact, the appetite is more or less completely lost, the tongue is coated, and the patient complains of chilliness and fatigue. A moderate fever may exist. Occasionally the disease is ushered in with a rigor, though rarely. In the most acute cases the apogee may be reached in forty-eight to sixty hours, the sufferer having almost constant stools with great pain, thirst becomes intense, delirium supervenes, and death may occur from the third to the fifth day. In less severe types the course may extend over several weeks, the frequency of the stools gradually lessens, the pain abates, temperature falls to normal, though the patient may remain weak and anemic for some time. A mild icterus occurs in some individuals during the course of an attack. Vomiting is not a prominent feature in this condition. The urine is diminished in proportion to the

severity of the malady, and a febrile albuminuria develops. Considerably more albumin is lost in the serous stools. In most cases lasting a number of days, the heart becomes rapid, the heart muscle becomes weak and irritable, so that a small, rapid pulse often occurs, and may persist for some time after convalescence is established. The most severe cases run a short course with a high mortality. The less acute forms may extend over a period of many weeks, emaciation progressing to a marked degree. In every epidemic, cases are met with in which the chief or even the only symptom is diarrhea, and but for their relation to other cases in the same locality, and the fact that the dysentery bacillus has been found in the stools of such individuals, their true nature would pass unrecognized. Sporadic cases of the same character are met with in temperate zones which run their course with little or no fever. Probably many of the diarrheas occurring in bottle-fed babies are of this character, as we now know that form to be which is most apt to occur during the summer months, and which is often called cholera infantum. Diphtheritic dysentery is merely one form of bacillary dysentery, in which the intensity of intestinal involvement is so great as to result in marked infiltration and necrosis of the mucosa. Apparently mild cases may quickly become grave by the development of gangrenous foci, or the case may have been of great intensity from its incipency. These latter are spoken of as primary diphtheritic or gangrenous types, the former as secondary gangrenous or diphtheritic dysentery. Shreds and sloughs of the mucosa may be seen in

the stools as well as pus and blood. Rarely a cast of the bowel may be passed. These cases, when well developed, belong to the most severe and fatal type, and though recovery may occur, it is not the rule; fall of temperature, collapse, dry tongue, coma—in short, the typhoid state precedes death.

The mortality statistics of epidemic dysentery are given by Vaillard and Dopter for the following countries: Japan, 24 per cent. (Shiga); Moscow, 12-17 per cent. (Rosenthal); Westphalia, 11 per cent. (Kruse); Toulon, 6-9 per cent.; Brittany, 20-50 per cent.; Finisterre, 50-60 per cent.; the difference in the severity of the disease being due, according to these authors, to differences in the virulence of the bacilli. Corney (Jour. London School of Trop. Med.; Austral. Med. Jour., June 15, 1912).

*Chronic dysentery* differs chiefly in the milder but more protracted course. The patient becomes weak, anemic, more or less emaciated, and presents an array of gastrointestinal disturbances in which diarrhea of the lienteric type is a prominent feature.

**COMPLICATIONS AND SEQUELS.**—A not infrequent complication is joint involvement. Some observers have dignified this condition by a special classification,—arthritic dysentery. This is not justifiable. The relationship was noted by Sydenham, who said “there was pain in the muscular parts of the body—especially at the joints—like the pain of rheumatism. Besides this, there was an inflammation of the fauces; like (but milder than) a quinsy.” He noted, too, that this tendency was more marked in some epidemics and during some seasons than in others. This has been confirmed by modern observers. The large joints particu-

larly are involved, but cardiac complications, *i.e.*, valvular involvement, play no part, though in any severe case of dysentery the heart muscle is affected to a variable degree. Other serous membranes may be attacked, however, pleurisy or pericarditis resulting. Peritonitis may occur without perforation, though, as a rule, it is due to separation of deep sloughs with consequent perforation. A periproctitis may be caused in the same manner. Thrombosis is a possible though not a common complication. Pyemic phenomena may arise, such as pyelephlebitis, mycotic abscesses in other organs (as the spleen, for instance, which may spontaneously rupture), septic nephritis or parotitis, with chills and fever. Since malaria may be a concomitant infection in some cases, an examination of a fresh or stained blood-smear should be made. Apart from the multiple abscesses of a pyelephlebitis, not a common complication, a single abscess of the liver is even less common in bacillary dysentery. In temperate climates there are no phenomena associated with an attack of this type of dysentery, which may be directly ascribed to the liver, enlargement of that organ and jaundice being so exceptional. In the tropics, however, the so-called “tropical liver” occurs so frequently that it is not surprising that the chronic congestion and enlargement become more pronounced in the course of an attack of dysentery. A heaviness in the right hypochondrium, with pain on pressure, and more or less jaundice are the rule. A rigor may bespeak the development of a liver abscess, but this latter often proceeds so insidiously as not to attract special attention.

Marcans identified hepatic abscess by the pain in the right shoulder, the leucocytosis with polynucleosis, and repeated X-ray examination. The first radioscopy was misleading. Repeated exploratory puncture was also useful. Zancarol was unable to discover the abscess in one case even with thirty punctures. In case of inversion of the viscera the diagnosis may be almost impossible, as in a case seen by Alvarez in which the patient was finally cured by resection of two ribs on the left side and evacuation of a large hepatic abscess. A. Chauffard (Bull. de l'Acad. de Méd., May 5, 1908).

Cases of dysenteric abscess of the liver in France which showed the same characteristics as the tropical abscess. It may follow a mild dysentery which may not have attracted attention, and it may run a latent course simulating a tuberculous process in the lungs, pneumonia, pleurisy or a suppurative hydatid cyst. In acute suppurative hepatitis with multiple abscesses, or an abscess with necrosis, the general symptoms may suggest typhoid fever or severe jaundice and the actual abscess be overlooked. The principal complications of these bacillary liver abscesses are adhesion between the focus or foci and the colon; perforation into the air-passages or pleura; pus collecting below the diaphragm, multiple abscesses in the left lobe of the liver, and postoperative bile fistula. Boinet (Bull. de l'Acad. de Méd., June 29, 1909).

In long-standing cases, where anemia has become marked, edema occurs, in part due to the blood change, and no doubt in part the consequence of a weak heart muscle. A rare complication of bacillary dysentery is multiple neuritis.

The sequelæ are not as common as one would expect from the nature of the disease. Many individuals never completely recover their health, espe-

cially after the more chronic forms of the disease, intractable dyspepsia and intestinal irritability remaining.

Of 71 cases of tuberculosis investigated 11 patients (15.5 per cent.) had a well-marked history of recent chronic dysentery. It is probable, that dysentery was a predisposing factor in a larger proportion of the fatal cases, because the fact of there having been repeated attacks of dysentery would not be noted in a necropsy report on a case of tuberculosis unless the connection was very strong or unless one were specially looking out for such cases. Gillitt (Indian Med. Gaz., Dec., 1910).

Cicatricial stenosis is rare. The symptoms are those of a slowly progressive and chronic obstruction of the bowel, swollen and tender abdomen, flatulency, paroxysms of intestinal colic, small and difficult stools, with increasing toxemia. Death may be due to obstruction or to some intercurrent malady. Prolapse of the rectum, hemorrhoids, proctitis, cystitis, chronic nephritis, anemia and edema may also be numbered among possible sequelæ. Relapses may occur during or even after convalescence, especially in those addicted to alcohol. Undue physical effort or the use of irritating food may invite reinfection.

Features of a relationship the writer has found to exist between a "crisis" or period of sudden improvement in cases of acute bacillary dysentery and the elimination of chlorides. Early in the disease there is oliguria. The elimination of urea is diminished in afebrile cases; that of chlorides is almost *nil* (0.2 Gm. in 1 instance), while that of phosphates is relatively but little decreased. In cases tending toward recovery there occurs a sudden increase in the urinary chlorides to above the normal amount, in addition to polyuria. While the salt lost through the alvine

discharges early in the affection may be considerable, and the intake is low owing to dietary restrictions, these circumstances do not wholly account for the low chloride elimination. The author concludes, therefore, that there is a systemic retention of chlorides in this affection. Successive injections of 150 and 200 c.c. of salt solution in an adynamic case of dysentery were badly borne, inducing restlessness and dyspnea. L. E. Bertrand (Bull. de l'Acad. de méd., Nov. 28, 1911).

**DIAGNOSIS.**—Bacteriological examination of the stools, while yielding definite results, is a difficult and time-consuming procedure. Agglutination of a known culture of the Shiga or Flexner-Harris type by means of the patient's serum is the most practical procedure. Both of these will react, the Shiga to a less extent than the Flexner-Harris, however.

Taken in conjunction, the iodine reaction of the polynuclear leucocytes and the production of nuclear pseudopodia in the polynuclears permit a rapid and differential diagnosis between bacillary and amebic dysentery. A well marked iodine reaction and the absence of nuclear pseudopodia indicate bacillary infection, while the exact reverse is indicative of an amebic infection. A mixed infection is indicated by the presence of positive reactions to both tests. The application of these two tests gives correct results in at least 90 per cent. of early cases. The iodine test is performed by incubating a drop of blood between a slide and cover glass for 1 hour to obtain adherent polynuclears, which are washed clean with a little normal saline. The 2 films of white cells are then mounted in 1 per cent. iodine in potassium iodide and the proportion of cells containing mauve colored droplets is determined, the size of the droplets being also noted. In bacillary infections from 60 to 80

per cent. of the cells will give the reaction, as compared with about 50 per cent. for normal persons. In some of the long-standing cases of amebic dysentery, in which there is marked ulceration and secondary bacillary infection, the iodine reaction will be found positive and in such cases the diagnostic value of the test is much impaired. G. M. Findlay (Lancet, Jan. 25, 1919).

As in the case of typhoid fever, in which J. McCray showed that it takes six days for agglutinins to develop, so in bacillary dysentery, this test can only be used after the sixth or seventh day. In the epidemic, asylum or institution type, bacillary dysentery is not difficult of recognition nowadays, and to these we are justified in adding the summer diarrheas of infants, especially occurring in the bottle-fed. The sporadic case, however, can only be suspected, more or less strongly, without laboratory diagnosis.

The writer holds *macroscopic agglutination* is more reliable than microscopic in the recognition of bacillary dysentery and detection of carriers. The test becomes positive by the 7th day, and was positive in 75 per cent. of cases examined early in the course of epidemics, though less frequently later. Guimaraes (Brazil-méd., July 12, 1924).

The author warns that a child with high fever, convulsions and diarrhea should be suspected of having bacillary dysentery, especially if the stools contain mucus and are blood-tinged. One negative laboratory report means nothing. A stool specimen should be submitted twice daily for at least 3 days. In the absence of an epidemic, the cases of non-specific enterocolitis so far outnumber the dysentery cases that serum treatment is not necessary until a positive diagnosis has been made. Connor and Bates (Proc. Intern. Conf. on Health Probl. in Trop. Amer., 1924).

Where gangrene of the intestinal mucosa supervenes, the peculiar odor, profound infection, and the passage of foul, necrotic sloughs or casts will serve to render diagnosis comparatively easy.

The diseases most often confounded with dysentery are carcinoma, polypi, and syphilis of the rectum; hemorrhoids and, in those returning from the tropics, bilharziasis. The following points should be remembered: 1. Amebic dysentery, unless skilfully treated at the beginning, runs usually a chronic course, while the bacillary form lasts only from four to eight days in mild cases and from three to six weeks in serious ones. 2. In the amebic form no bacilli can be found except under the rare conditions of a mixed infection. 3. Toxic symptoms, such as high fever, rapid emaciation, and nerve complications, exist in bacillary dysentery, but not usually in the amebic form. 4. Liver abscess is a frequent complication of amebic dysentery, and does not exist in the unmixed bacillary form. Sandwith (Lancet, Dec. 7, 1907).

Case of dysentery due to the rare monad, *Balantidium coli*. The disease has been attributed particularly to the habitual consumption of fresh sausage, the parasite being commonly found in the intestine of the hog. Those who handle hogs or assist in the preparation of hog sausage are liable to contagion. Taboadela (Sanidad y Beneficiencia, Jan., 1911).

An outbreak of bacillary dysentery studied by the writer presented the following features: (a) Sudden onset and brief duration; (b) evidence that the infection was water-borne; (c) Shiga's bacillus as the infecting agent in all cases; (d) evidence of the persistence of Shiga's bacillus when experimentally introduced into water and food; (e) noteworthy results of agglutination tests when applied both to dysentery convalescents and to those who had presumably been exposed but had escaped illness. G. S. Buchanan (Lancet, Aug. 10, 1918).

Many commonplace disorders simulate dysentery: Syphilitic ulceration of the rectum; large fungating malignant growth in the rectum; advanced tuberculosis of the lungs, with extensive tuberculous ulceration in the small and large bowel; schistosomiasis infection only; paragonimus dysentery; heterophyses dysentery; ankylostomiasis; balantidial dysentery, and pseudodysenteries, such as from foreign bodies impacted in the rectum above the anus. Low (Brit. Med. Jour., Feb. 21, 1920).

The form of dysentery due to *Balantidium coli* was observed by the writers. It requires 8 or 9 months to develop. Their case also yielded to **emetine**. Vedel and Baumel (Arch. des mal. de l'app. dig., No. 4, 1922).

A similar case is recorded by the writer which rapidly improved under **benzyl benzoate**. Haughwout (Philip. Jour. of Sci., June, 1920).

As to the clinical differential diagnosis of amebic and bacillary dysentery, Blackham offers the following points:

#### AMEBIC.

1. Always chronic in its course.
2. Pyrexia rare.
3. Toxic symptoms not present except when there is liver abscess.
4. Liver abscess occurs in about 16 per cent. of cases.
5. Small intestine frequently attacked.
6. Undermined ulcers present.

#### BACILLARY.

1. Acute in onset and running a rapid course.
2. Pyrexia common.
3. Toxic symptoms usually present.
4. Liver abscess never occurs.
5. Disease confined to the large intestine.
6. Ulcers usually formed on surface folds of intestine.

**ETIOLOGY.** — *Season.* — In temperate zones dysentery is far more common in summer than during the fall, spring, and winter, in the order mentioned. In the tropics, where the seasons are marked according to rain-



fall, the temperature being more equable, the incidence of dysentery is greater after torrential rainfalls, the probable explanation being the pollution of sources of drinking-water.

*Soil.*—Infected soil may continue to harbor the specific organism and give rise to recurrent outbreaks; how long it remains viable in soil is not definitely known. Both in temperate and tropical regions, marshy soil seems more prone to invite outbreaks than dry regions. Fecal pollution is naturally a most important element.

*Food and Drink.*—Famine or the use of improper foods, this latter especially in the tropics, may determine outbreaks. Fecal pollution of drinking-water or the transference of infection to food by flies are self-evident possibilities in causing more or less widespread outbreaks.

*Exhaustion and Exposure.*—Insomnia, prolonged and exhausting effort or profound worry, all play a rôle. Fatigue for any reason and severe exposure may so lower resistance as to encourage the development of dysentery, which, under these conditions, is apt to carry with it a high mortality.

*Other Diseases.*—Dysentery may occur as a terminal infection among the aged or children, especially in institutions, or it may complicate depraved states during the course of or as a terminal infection in other diseases, as in pneumonia, tuberculosis, Bright's disease, cystitis, etc.

*Age.*—No age is exempt; even the fetus *in utero* has been found affected by Marckwald. (Münch. med. Woch., 1901, p. 1920). Children at birth have been found with an infection which developed during intra-uterine life, having been contracted from the

mother who was ill at the time with dysentery. The summer diarrheas of infants have been shown by Duval and Bassett ("Studies from the Rockefeller Institute," 1904, ii) to be due to one of the varieties of the *Bacillus dysenteriae*; so, too, with the cases of so-called asylum dysentery reported by Vedder and Duval (Jour. of Exp. Med., 1902, vi, No. 2), and with the institution outbreaks in homes for the aged. In the tropics a large part of the high mortality rate among children is due to dysentery.

*Sex.*—Not a factor *per se*, only in so far as habits and greater exposure increase the susceptibility of the male.

*Race.*—No racial predilection. All people of all ages in all climes would best express the situation, the general predisposing factors previously enumerated being the important determinants.

*Occupation.*—The working classes being more exposed through fatigue, dietetic restriction or errors, and poor hygienic environment than the well to do, are naturally more prone to the disease. In country districts the lack of sanitation invites a more ready development than in cities, while in those exposed to great heat, as engineers, firemen, and cooks, are more liable in consequence.

**BACTERIOLOGY.**—One time the colon group of organisms were believed to play a rôle in the production of dysentery, and it is possible that their increased pathogenicity in the presence of inflammatory states of the bowel may add to the symptoms, but they do not occupy any direct relation in an etiological sense. Despite Shiga's painstaking work published in 1898 (Centr. f. Bact., 1898, xxiii, p.

599, and xxiv, p. 817), and almost at once confirmed by other observers, even in 1902 Bertrand (Rev. de méd., July 10, 1902) stated his belief that dysentery was caused by an increase in virulence of the micro-organisms normally inhabiting the intestinal tract, and not to any specific germ. So, too, Booker believed with respect to the summer diarrheas of children. These he ascribed to a variety of bacteria, the most important in his opinion being the streptococcus and proteus vulgaris. Calmette (Archiv. de méd. navale, Sept., 1893) also found a coccus having all the properties of *Streptococcus erysipelatosus* and the *Bacillus pyocyaneus*, both regarded by him as causing dysentery among the natives of Cochin China. A similar enterocolitis has been described by Adami and Lartigau as occurring in the northern part of the United States and in Canada, and they also isolated the *Bacillus pyocyaneus*. I. F. Barker, of Johns Hopkins, and others have also reported several cases due to the same organism. Calmette succeeded in producing hemorrhages and ulceration of the stomach and intestines by the injection into rabbits of a culture of *Bacillus pyocyaneus*. Enteritis and enterocolitis are undoubtedly due in some instances to subvarieties of the colon group, notably the organisms of Gärtner and Escherich.

Studies of 300 stools during an epidemic which broke out simultaneously in several small foci in a military district in the late summer of 1917, established clearly the rôle of Shiga's bacillus in the more severe and clinically typical cases, while in the mild the Shiga organism was generally wanting and was replaced by aberrant bacilli of the dysentery group. The Shiga bacillus was isolated in large numbers from 43

cases, and in dishes of lactose litmus agar at times almost completely replaced the normal intestinal flora, no colonies of colon bacillus being found. In 26 milder cases a number of different forms of organisms were found, which did not correspond to any of the classical types of dysentery bacillus and never occurred in the severe or fatal cases. Bezançon, Ranque, Senez, Coville, and Paraf (Bull. de l'Acad. de Méd., Mar. 26, 1918).

The first studies of a definitely practical character, however, emanated from Shiga, as already stated. In his paper in 1898, on the epidemic form of dysentery occurring in Japan, he insisted that an organism, to be regarded as the direct cause of dysentery, must be constantly present in cases of dysentery, yet not normal to the host, and that it should be pathogenic and capable of causing lesions in experimental animals similar to those occurring in the one from which the culture was made, and, finally, in man, it should agglutinate with the blood of those harboring the disease.

Of late years the view has become more generally accepted that no organism is under all conditions fixed and definite, but that gradations exist, so to speak. For instance, from the colon group on the one end to the typhoid group on the other, innumerable variations pertain; so, too, with the streptococci and all other micro-organisms. Nor is the dysentery bacillus an exception. Here, too, a group arrangement exists. Two predominant types, however, have been described, the first by Shiga, which was isolated from the patients suffering with dysentery in Japan, and the second Flexner obtained from dysenteric cases in the Philippines. This is spoken of as the Flexner or Manila

type. It has since been shown, however, that both of these types occur not only in Japan and the Philippines, but also wherever dysentery occurs, and that the two types may even be associated in the same individual. No differences can be detected in the morphology of various types. They are rod-shaped, rather short, somewhat resembling the typhoid bacillus, though a little fuller and the ends are round. Duval and Vedder were able to demonstrate flagella, but it is now generally accepted that only very young cultures develop motility in the organisms. They stain readily, often irregularly, and decolorize by Gram's method. They grow readily upon the culture media most commonly employed in laboratories, the growth being best obtained at a blood temperature. They do not peptonize. They do not coagulate milk, which becomes at first slightly acidified and later amphoteric or faintly alkaline, indol production being present in some and absent in others. Probably the widest differences exist in their fermentative properties, though gas is not formed in any of the sugars. They also differ in their property of agglutination. This is so marked that Kruse was led to describe what he termed true and false dysentery bacilli. This is, however, unjustifiable, as all of the species of virulence of a common type and the variation in agglutination are but a matter of degree. It has been found that the power to produce agglutination may be increased by successive cultivations on various media. It has been noted, however, that though cultivation is possible through perhaps several generations, it is not possible to continue them indefinitely. This

varies with the type of organism, some showing a property of growth even after many transplantations. It may be stated, however, that the culture media should be slightly alkaline, as even minimal traces of acids seriously militate against the growth; consequently sugar media, particularly if fermentable, will not prove satisfactory, owing to the acids resulting from the sugars. The various organisms are not particularly resistant. They are at once destroyed by 5 per cent. of carbolic acid solution and 1:2000 corrosive sublimate. They are easily destroyed by saprophytes, and after ordinary conditions of soil or water contamination it is scarcely possible that they ever exist over two weeks.

The virulence of the various organisms is greatly diminished by culture. Though, as was shown by Marmorek in the case of streptococci, their virulence can be greatly increased by successive passage through laboratory animals, especially the guinea-pig. It seems, however, that an even greater degree of virulence can be obtained if intermediate cultures are made before transplantation from animal to animal. This seems peculiarly suggestive in the light of various outbreaks which occur from time to time, for it is probable that the organisms may be kept viable or have their virulence increased through the intervention of some of the lower animals.

Immunization has been shown to be practical in animals; but as each immune serum best protects against the type from which it was prepared, a therapeutic serum to be of any value had best be polyvalent, that is, made from many strains.

*Human Bacillary Dysentery*.—Owing to the rapidity with which the dysentery bacillus is destroyed, cultures should be made from perfectly fresh fecal material, though scrapings from the mucosa may be made at necropsy and growth will result if this be done within twenty-four hours after death. Careful selection should be made from the stool, preferably from clumps of mucus, with or without blood. This is placed in sterile salt solution or bouillon, thoroughly agitated or broken up with sterile glass beads, allowed to sediment for a few moments; then agar tubes may be inoculated successfully, the object being to effect dilution. These are then poured into Petri dishes and incubated at 37° C. for about eighteen hours. A very small, pearl-gray colony is then selected and transplanted by means of stabbing a glucose-agar tube. The plates should be kept at room temperature for purposes of further comparison, and the stab cultures should be examined after six hours at 37° C. Only those tubes are subjected to further subcultures and agglutination tests which fail to show gas-bubbles.

The discovery that the dysentery bacillus is the immediate etiological factor in dysentery, whether occurring in the tropics, subtropical or temperate zones, whether the disease occurs in epidemic form, institution outbreaks or sporadically, and, likewise, that it is the cause of the prevalent summer diarrheas of infants, naturally led to a query as to its source, mode of conveyance, and possible saprophytic character. These questions cannot be unequivocally answered at present. Except in those instances in which infection can be

clearly traced from infected persons, its source and mode of transference are unknown. It is found in the recent fecal discharges of infected individuals and at necropsy; in the mucosa of the bowel, especially in the large intestine, where it penetrates into the crypts, but outside the body, it is rapidly overcome by other organisms. This latter fact, and its intimate relation with the mucosa, do not well accord with the view that it is adapted to grow elsewhere. It has been recovered from the stools of apparently healthy children by several observers; but as it may also be found in the stools of those apparently well, but exposed to infection during local or widespread outbreaks, just as cholera vibrio have been found in the stools of those exposed but unaffected during outbreaks of cholera, it cannot be denied that it may exist as one of the vast numbers of flora inhabiting the intestine of man, assuming pathogenetic properties under favorable conditions the nature of which we are at present in doubt. The prevalence of summer diarrheas of children and the etiological relationship to them which the dysentery bacillus group bears, and its similar intimate relation in causing institution and asylum outbreaks, argue for this hypothesis, and so too does the development of dysentery as a terminal infection in those in advanced stages of Bright's disease, chronic heart disease, diabetes, hepatic cirrhosis, malignant disease, and the like.

We know beyond cavil that pneumococci, various pus organisms, tubercle bacilli, meningococci, even typhoid bacilli, as well as the spirillum of cholera, as previously stated,

may occur, some of them as constant inhabitants of the human body, without any evidence of morbid activity. It is very possible, therefore, that everyone is a "potential carrier," though in the more restricted sense carriers have only been proved to exist in the persons of those more or less recently actively infected. Local outbreaks have been traced to such individuals. It is not known how long the bacilli remain active in those who have had the disease, but there is no doubt that it may extend over many months.

Carriers may be divided into two great classes. The first class consists of healthy persons, who have never suffered from the disease and show no signs of ill health, but nevertheless harbor and scatter the specific organism. In the instance of bacillary dysentery this class is small and unimportant. The author has never found a single case, but Conradi, Collins, and Mayer have been able to demonstrate such conditions in both children and adults living among those affected with the disease. In the second class are people who have had the disease and are thereafter unable completely to eliminate the infection. These incomplete convalescents form a high proportion of the cases of dysentery actually occurring. Macalister (Brit. Med. Jour., vol. ii, p. 1506, 1910).

The existence of healthy carriers of *B. dysenteriae* in the Philippine Islands was demonstrated by the writer.

The proof of this proposition was carried out by isolation of cultures which, according to the standard methods of identification adopted, proved to be *B. dysenteriae*.

In the course of 3328 examinations conducted for the purpose of settling the question, 14 carriers were found, of whom 7 harbored the Shiga type, 6 the Flexner type, and 1 both the Flexner and Shiga types. A. Vazquez-Colet (Philippine Jour. of Sci., Oct., 1925).

**MORBID ANATOMY.**—From the foregoing, in order to establish some type as a basis, it appears advisable to consider, first, the lesions occurring in the severer forms of dysentery of the epidemic type, for of their true nature there can be no doubt. With these in mind, it will be possible to correlate those cases occurring especially in temperate zones, not necessarily grouped, often isolated examples in fact, such as one meets with in the summer diarrheas of infants. Clinically, there are acute and chronic types of dysentery. The most marked lesions occur, as one would expect, in the epidemic and endemic forms, and, naturally, the severity and duration of the attack are factors which determine the extent of bowel lesion. In the most acute cases, where death supervenes after an illness of a few days, the mucosa of the large intestine is swollen, injected, often of a very deep red color. The process begins on the tips of the mucous folds, then spreads to other portions. Apart from this more or less general hyperemia, minute extravasations and hemorrhagic foci may be seen, and the wall soon becomes edematous and covered with mucus. A pseudomembrane forms almost at once, at first irregular, patchy, but may become general. Early in the stage of its formation it may be wiped off, but in all likelihood, owing to the activity of the various pathogenic organisms present, foci of ulceration occur. In the most intense cases these ulcers may penetrate to and even through the serosa, purulent peritonitis resulting. Usually, however, they dip down to the muscular coat. Mixed infection and dehiscence of the more or less necrotic mucosa

and false membrane give rise to these irregular, often extensive ulcers. The solitary lymph-follicles are swollen, often softened and may break down. The small intestine, always less involved, is more or less hyperemic, and the ileum, which is the region of the small bowel most markedly affected, may present the same character of pseudomembrane, even ulceration, and the lymph-apparatus throughout the small intestine may become swollen and in the ileum necrotic, as was noted in the large intestine. In the less acute cases the loss of continuity of mucosa is small, mere erosions, but the hyperemia is marked. In chronic cases the bowel wall, especially the wall of the large bowel, becomes thick, indurated; the serosa thickened in patches, often pigmented, and the mucosa beneath also pigmented, mark the site of recent ulceration. Healing by cicatrization may slowly progress in areas, with ulcer formation in other places, and more or less distortion; even stricture may result, or the bowel function be permanently modified in consequence of the changes resultant upon the various lesions. The bowel wall may undergo amyloid change due to prolonged suppurative lesions. Microscopically, the pseudomembrane is seen to consist of fibrin, entangling erythrocytes, and cells undergoing degeneration, the whole upon a mucosa undergoing coagulation necrosis. Hemorrhagic extravasations and accumulations of Unna's plasma cells, small round cells, polymorphonuclear neutrophiles and eosinophiles, and more or less degeneration of submucosa and muscularis complete the picture. Abundant bacteria can be seen in appropriately stained sections,

but cannot be recognized, except possibly the streptococci. The epidemic form, both in adults and children, presents a common type, but those forms of bacillary dysentery occurring clinically as summer diarrheas of infants vary much. There may be merely hyperemia and edema of the large bowel, much less marked in the small intestine, with or without pseudomembranous formation, while in others hyperplasia of the lymphatic apparatus constitutes the chief feature, and in some the pathological changes are very slight, scarcely amounting even to hyperemia.

The bowel lesion results, in all probability, not from direct action of the bacilli, but from their toxin, which is eliminated by the bowel, after absorption into the blood. Sweet and Flexner have shown that the toxin enters the intestine in large part with the bile, for in experimental animals possessing a biliary fistula, lesions of the bowel are either prevented or at most are very trifling in character.

**PROPHYLAXIS.**—It is of importance to avoid the use of alcohol, in the tropics especially. Even in temperate zones the intemperate seem more prone to infection. All discharges from a patient should be disinfected. Neglect of this procedure may invite a widespread outbreak, especially where subsoil and water contamination are possible. Fatigue and exposure to heat or dampness increases one's susceptibility. Flies may spread the disease unless the dejecta are covered prior to disinfection. All excesses in food or the use of uncooked vegetables, celery, cress, salad or fruits may act as predisposing factors, or the uncooked foods may actually be the means of direct

infection through contaminated soil, just as we know them to be in the case of typhoid fever. The value of serum from horses immunized against dysentery, as well as bacterins, used prophylactically, are too recent to permit of an authoritative statement.

The serious consequences from dysentery vaccines led the writer to try the effects of **sensitized vaccines**. The vaccines were stock ones of Shiga or Flexner strains sensitized with the Lister Institute antidysenteric serum. The single doses of these vaccines never exceeded 100 million. In most cases the results were very satisfactory. Leonard Rogers (Brit. Med. Jour., Jan. 1, 1916).

Dysentery **vaccination** is of great importance practically. Since 1912, he has prepared a mixed dysentery vaccine, and also a vaccine containing the mixed vaccine plus typhoid, paratyphoid A, paratyphoid B. Dysentery vaccine of this type should be prepared with a carbolic salt emulsion from agar cultures without heating, or peptone water cultures. Many strains of Shiga-Kruse bacillus should be inoculated in rabbits, and the least virulent, provided it be rich in antigen, should be kept permanently as a stock culture. Broth cultures should not be used. Castellani (Brit. Med. Jour., Feb. 26, 1916).

Proper disposal of the human dejecta advised, together with adequate screening. T. J. Carey Evans (Brit. Med. Jour., Mar. 31, 1917).

**TREATMENT.**—Whether mild or severe, acute or chronic, absolute **rest in bed** is necessary. A firmly applied **flannel binder** should be employed, with or without **hot applications to the abdomen**, either dry or moist, and the patient kept warm and free from all sources of irritation. Thirst is a very annoying symptom, but if the patient is vomiting absolutely nothing should be given by mouth. Fluid may be administered by **hypodermoclysis**

or, if the rectum will tolerate it, by **enema**.

The **diet** is an important factor. Those who take it well should be given predigested milk or whey, but special care should be exercised to insure milk beyond suspicion. Lime water or barley water may be added with advantage, unless the milk is predigested. Rice, barley or oatmeal water or albumin water, strained gruels or chicken or other meat broth thickened with some cereal and strained should constitute the sole diet of those unable to take milk or as variants with a milk diet. All alcohol should be avoided except where prostration is marked, when **wine whey**, or **brandy and milk** may be given, also **aromatic spirits of ammonia** with a drop or two of **chloroform** in  $\frac{1}{2}$  dram (2 Gm.) of **Hoffman's anodyne**. Even after convalescence has been established, it is important to maintain the greatest care in the matter of **diet**, adding very gradually the cereals, vegetables, and finally the meats.

Early in the course of an attack, **salines** may be given, **Glauber's** or **Rochelle salt** in one dose of  $\frac{1}{2}$  to 1 ounce (15 to 30 Gm.) in the morning, or, if free purgation with a change in the character of stools is not produced, this may be repeated at four-hour intervals for twelve to twenty-four hours. One dram (4 Gm.) every hour may be given instead of the above. In some instances this will effect a prompt disappearance of blood and mucus. In the more severe forms this method usually fails and in the gangrenous stage should not be employed at all. **Castor oil** in 1-ounce (30-Gm.) doses may be given and repeated in eight to twelve hours, or **calomel** may be given in a single

large dose, followed in six to eight hours by a **saline**. Repeated doses of calomel are apt to add to the misery of an already inflamed anal region and rectum. Small doses of **bichloride of mercury**, gr.  $\frac{1}{100}$  to  $\frac{1}{60}$  (0.00065 to 0.001 Gm.) may be given every two hours.

**Adrenalin** by the mouth quiets the abdominal pain and tenesmus of bacillary dysentery. When given every 1 or 2 hours it is possible to keep the patients entirely free from pain. In an experience with 300 cases he found that even enormous amounts were borne without appreciable by-effects. Addition of adrenalin to tepid saline for flushing the bowel had a remarkably favorable action. Gröer (Münch. med. Woch., Apr. 6, 1915).

Large doses of one of the **bismuth** preparations with **paregoric** or **laudanum** by mouth will often give some comfort, but it seems wiser to employ **morphine** hypodermically in doses of gr.  $\frac{1}{4}$  to  $\frac{1}{3}$  (0.016 to 0.02 Gm.) in an adult, every three or four hours for the relief of the tormina and tenesmus. When the tenesmus is urgent, a **suppository** of **cocaine** or **opium** may be used, followed by a low **starch-water enema** containing about 30 drops of **laudanum**, or **bismuth** suspended in acacia solution may be used. While **ippecacuanha** and **emetine** (see article on EMETINE, this volume) are of less value in the bacillary form than in amebic dysentery, they may be tried, but unfortunately no single medicinal treatment will give the same result in every case. When given from the beginning of an attack these two agents are apt to be of most service, though even in well-marked and severe cases, especially in the catarrhal stage, they sometimes act well. If the patient has been previously

constipated, a dose of salts or oil should be given first. Nothing should be given by the mouth for several hours preceding the **ippecacuanha**, which is best administered at bedtime in salol or keratin-coated pills, to insure their passage into the duodenum before solution occurs, lessening the likelihood of nausea and vomiting. From 60 to 90 grains (4 to 6 Gm.) may be given at the first dose, less each evening for a week, then daily doses of  $\frac{1}{2}$  dram (2 Gm.) in divided doses should be given for at least two or three weeks. Where the pills cannot be prepared one may give 30 to 60 grains (1 to 2 Gm.) of the powdered drug in the form of a bolus, to be repeated every six to eight hours. If vomiting occurs it may not render subsequent administration impossible. Precede the dose by placing a **mustard plaster** over the epigastrium and give a hypodermic of gr.  $\frac{1}{4}$  (0.016 Gm.) of **sulphate of morphine** or **laudanum**  $\text{mxxx}$  (1.8 c.c.) by mouth. When the passages begin to show fecal material, betterment is near at hand and the dosage and frequency should be reduced, but 20 to 30 grains (0.3 to 2 Gm.) a day should be continued for a couple of weeks. For children, much smaller doses should be employed. It is not to be given to pregnant women without explaining the risk of abortion from possible repeated vomiting, nor to those who for any reason are devitalized, as the actively tuberculous, for instance.

The **ippecac** treatment of dysentery caused by protozoa should not on light grounds be set aside in favor of any other, but in using this treatment great care should be taken to make sure that the dysentery is truly caused by protozoa and is not



bacillary, and also to obtain an ipecac that is shown by actual analysis to contain its proper amount of emetine, and, when this is not possible, to insist upon obtaining the Brazil root. E. B. Vedder (Military Surgeon, Sept., 1911).

The writer warns against treating bacterial dysentery with astringents from the beginning. The treatment should always start with a dose of **castor oil** or with **magnesium sulphate** in dram (4 Gm.) doses every hour, or 2 drams (8 Gm.) every 2 hours, for 24 to 48 hours. Then astringents should be given in massive doses, *e.g.*:—

*R. Bismuthi sub-*  
*nitratis* ..... gr. xxx (2 Gm.).  
*Liquor morphinae*  
*hydrochloridi*  
(B. P. 1 per  
cent.) ..... m̄ij (0.12 c.c.).  
*Aqua chloroformi*  
q. s. ad ..... f̄ij (30 c.c.).

M. Sig.: To be taken every two hours, day and night, for several days.

**Irrigations** are generally badly borne in acute cases, but in the sub-acute cases the author finds effective a solution of **gallic** or **tannic acid** and **opium** in water, and in very chronic cases a 24-grain to the quart **silver nitrate** solution. In the serum treatment, he uses a **polyvalent serum** in large doses; it should always be supplemented with the internal treatment already described.

In polyarthritis from dysentery, in which the salicylates have practically no action, the **serum** and occasionally the **vaccine** treatment are useful. Aldo Castellani (Jour. of Trop. Med. and Hyg., Sept. 1, 1917).

Whenever possible, **enemas** should be resorted to. Even though the anal region be irritable, a suppository of **cocaine** and **opium** will usually obviate all pain or, at least, make it bearable. A preliminary **enema** of physiological **salt solution**, 2 or 3

quarts, should be given, the patient lying on the right side, hips elevated and head low. This is to be followed by an **enema** of 3 quarts of a 1 per cent. solution of **quinine bimuriate with urea**. This causes some pain at first, but its anesthetic effect is soon felt and, being to some extent a parasiticide, it has a double range of usefulness. Since in many cases the disease is confined to the large bowel, the involved area can be thus directly treated. In well-advanced cases where there is likelihood of softening and extensive ulceration of the bowel wall, **enemas** are contraindicated, as the risk of perforation cannot be denied. Nor would they be of value in treating that part of the morbid process when the small bowel is involved. Saturated **boric acid solution** or a 1 per cent. or 2 per cent. **solution of salicylic acid** are distinctly of less value than quinine **enemas** in any case. Any **enema** employed should be given at body temperature.

In the treatment of bacillary dysentery and on the basis of wide experience in the British Salonika forces, the writer recommends the following: In acute and severe cases all patients are given 15 c.c. (½ ounce) of **castor oil** on admission and, beginning 8 hours later, receive 8 Gm. (2 drams) of **sodium** or **magnesium sulphate**, which is repeated every 4 hours as long as the mucous stage lasts. When the mucus disappears the saline is given in just sufficient amount to secure a soft movement. Intestinal lavage with solutions of **eusol**, **potassium permanganate**, **protargol**, or **normal saline** are given night and morning if the patient is relieved by their use. **Opium** **enemas** and astringents by mouth are irrational. Anti-dysenteric **serum** should be begun at once and given intravenously. To

avoid the severe primary reactions which occasionally occur 2 c.c. (30 minims) should be injected at once and the remainder slowly run in after an interval of 10 minutes. Larger doses than usually prescribed should be used, ranging from 60 to 80 c.c. (2 to 2½ ounces), and should be given twice daily. In most of the very toxic acute cases the greatest danger seems to come from dehydration of the tissues and this can be largely overcome by the use of intravenous injections of 150 to 300 c.c. (5 to 10 ounces) of normal saline immediately following each dose of serum, or of 5 per cent. solutions of **glucose** in distilled water. Important in all forms is the proper regulation of diet, not only during the acute stage, but also when the patient is convalescent. In the beginning it should consist of albumen water, gruels, and tea sweetened with lactose. During recovery the diet should be slowly changed to contain **arrowroot**, **Benger's food**, **malted milk**, **sour milk**, and **diluted fresh milk**, **lactose** in the foods. Progress to full diet should be made very slowly. Duncan Graham (*Lancet*, Jan. 12, 1918).

The writer obtained excellent results with **calcium chloride**. He injected 10 c.c. (2½ drams) of a 10 per cent. solution twice daily and added **morphine** subcutaneously. Teodosijevits (*Deut. med. Woch.*, Sept. 25, 1925).

**Serum therapy** has a limited range of applicability, but has been of some value when employed in the early stages. Shiga has prepared an immune serum, so called, by repeated injections of polyvalent strains of the dysentery bacillus into a horse. Doses of 20 c.c. to 30 c.c. of the immune horse serum should be injected two or three times a day for several days, smaller doses in children.

**Serum** of horses immunized against the bacillus of dysentery possesses antimicrobial and antitoxic properties which render it useful in thera-

peutics. This serum is proving to be almost specific in the treatment of bacillary dysentery. Its effects are the better the earlier it is used, although it has proved effectual even as late as the sixteenth day. Prolonged and chronic dysentery is also amenable to this serum treatment. These results were practically constant in 96 cases of severe dysentery treated with the serum alone, the number of stools ranging from 15 to 288 a day. The amount injected ranged from 20 to 100 c.c., and the injection was sometimes repeated after twenty-four hours, and again a third time in the most threatening cases. The Shiga-Kruse bacillus had been used to immunize the horses, but the serum proved equally effectual against this and against the Flexner bacillus. The curative action of the serum is so prompt and certain that its prophylactic use seems hardly necessary. Vaillard and Dopter (*Annales de l'Inst. Pasteur*, vol. xx No. 5 1906).

**Polyvalent antidyentery serum** was administered to 13 children by the author; in 2 the dysentery was caused by the Shiga bacillus and in the others by the Flexner bacillus. The mitigation of the symptoms after the injection of serum was rapid. All the patients promptly recovered. P. Coyne and B. Auché (*Bull. de l'Acad. de Méd.*, Oct. 1, 1907).

The **serum therapy** of dysentery was begun by the writer in 1903. He first injected horses with killed cultures of a dysentery bacillus which he obtained in Japan, and later injected living organisms. Todd then elaborated a pure, antitoxic serum by injecting horses first subcutaneously and then intravenously with dysentery toxin. Other investigators, among whom may be mentioned Kruse, Vaillard, Dopter, Krauss and Doerr, confirmed these findings. By means of serum therapy the mortality of diseases was reduced to less than 17 per cent. of the former death rate. Since 1906 numerous investigations along the lines mentioned were car-

ried out. Horses were injected intravenously with a mixture of various strains of domestic dysentery bacilli. Alkaline broth was first injected under the skin, and then intravenously. The injections were made every two or three weeks, since it was determined that injections at shorter intervals frequently killed the animals. Commencing with an initial injection of 0.1 c.c. of the culture, the amount injected was increased until finally as much as 100 c.c. could be given. In the beginning a large number of the horses were killed by anaphylactic phenomena, but later this result was avoided by the antianaphylactic method of Besredka. The entire immunization stretched over a period of eight months. The horses are then bled, 8 liters of blood being withdrawn every four days until 24 liters of blood are taken. The horses receive a rest of about twenty days, and the injections are then begun again. The serum is preserved with 0.5 to 1 c.c. trikresol. The serum obtained from the blood will give agglutination up to 1:1000 immediately, and 1:2000 within three hours. It was possible by means of an antigen prepared from dysentery bacilli to obtain complement fixation. The antitoxic value of the serum was obtained by first determining the lethal doses of old and fresh cultures of Shiga bacilli and then injecting various mixtures of the toxin and antitoxins. Animals injected with the mixture did not succumb. It was possible by means of 1 part of serum to neutralize 10 times as much toxin. These experiments were carried out on rabbits, and it was determined that the protective properties of the antitoxin were definite and unmistakable. M. Shiga (*Ann. de Biol.*, t. i, No. 2, 1911).

The results recently obtained with **serotherapy** in the Shiga type of dysentery in eastern Austria are fully on a par with those of the antitoxin treatment of diphtheria. The writer has recently controlled 2000 cases during the past year. This could also be contrasted with a large number

of cases otherwise treated. The mortality of the cases treated with **anti-serum** was between 9 and 10 per cent., while that of the material otherwise treated was between 19 and 20 per cent. One condition of success was that the serum be given as early as possible, when its beneficent action was at once evident in the abortive course of the disease. The serum is essentially antitoxic. Krause (*Deut. med. Woch.*, March 7, 1912).

Many good reports on the **serum** treatment have been appearing. Job (*Arch. de méd. et de pharm. milit.*, Apr., 1921) states that dysentery due to the Flexner type will usually subside whether serum is given or not, but the **serum** against the Shiga type is necessary and valuable. Anti-Shiga serum has no effect on Flexner dysentery, while anti-Flexner serum is ineffective when dysentery has already set in. The anti-Shiga serum should be given at once, before the existing type is known, as it may save the patient's life. He advocates a **milk** diet, though in simple colitis milk is contraindicated. Tentative emetine treatment is disapproved of, and he is rather sceptical of good results from appendicostomy in the chronic cases. Lornie and D. E. Jones (*Brit. Med. Jour.*, June 17, 1922) reported that in the preceding year 728 persons in mental hospitals were attacked by dysentery, and 126 died. In their own institution they used in 10 cases, mostly severe, **serum** prepared by injecting horses with cultures of Shiga, Flexner, and Kruse bacilli. The dosage was from 25 to 40 c.c. Prompt and marked improvement resulted.

The **antidysenteric serum** should be given in all but the mild cases. Its value rapidly lessens with delay. Sixty, 80 or 100 c.c. may be injected subcutaneously. Often a single dose suffices. In urgent cases of choleraic type the serum should be given intravenously and combined with **hypertonic saline solution**. Best results are to be expected from a serum containing exclusively Shiga or Flexner antibodies, according to the type of infection, but in practice no time should be lost by waiting for the laboratory report. A. G. Phear (*Lancet*, Aug. 2, 1924).

A serum is also furnished by the Pasteur Institute and the Lister Institute. The injection of attenuated and dead cultures into the bodies of laboratory animals confers an active immunity upon them, but the injection of dead bacilli (**bacterins**) into man causes a sharp local reaction after the first dose, with more or less constitutional disturbance in most instances and some febrile reaction, just as we know it in the case of prophylactic injections of typhoid bacterins. They have not been employed sufficiently to enable one to speak with any degree of certainty as to their protective value, and, again as in typhoid fever, bacterins used therapeutically are almost without influence and certainly of no demonstrable clinical value. (See article on BACTERIAL VACCINES in the second volume.)

Experiments on the **vaccination** of full-grown mice by feeding them with bacilli of dysentery of the Shiga type, both living and dead. One single ingestion of this dose is insufficient to bring about immunization; an immunity is only conferred with weaker doses when they are repeated daily for a week. The immunity is not complete until about the end of twelve days and it usually lasts for a month. From the first to the twelfth days, while the state of immunization is in process of development, a "negative phase" is induced, and the animal is more sensitive than the control mice to an ordinary fatal dose. Similar results were obtained with living bacilli. M. Dopter (Lancet, June 6, 1908).

The writer has used a **mixed polyvalent vaccine** in East Africa with favorable results. Kauntze (Jour. of Hyg., Feb., 1920).

An epidemic is described by the writer which recurred for several summers in 2 Swedish sanatoriums and was ultimately checked with an **auto-**

**genous vaccine**. A brief immunity seemed to be conferred. Benefit was most marked in treating the chronic cases. The Y and Kruse E types of organisms were concerned. Karström (Upsala Läk. Förh., Feb. 1, 1921).

**Chronic Dysentery.**—**Rest** in bed, a very simple **diet** of farinaceous food, creamed potatoes, cereal broths, peptonized milk, gruel and eggs. Milk is often poorly borne, and, even when peptonized, curds may form and add to the irritation present. In such instances give no milk at all. Boiled, aerated water or pure water from any source may be given, unless there is much vomiting; then give nothing by mouth. **Bismuth** and **opium** are the best drugs to give, but, on account of the chronicity, a word of caution against the possibility of forming the opium habit is in order.

**Rectal and colonic irrigations** are of great value; the same caution to be observed as in acute cases.

Eleven cases of dysentery were successfully treated with **irrigation** of an emulsion of **creosote** prepared by adding to a quart of water, with which the yolk of an egg has been mixed, a dram of 10 per cent. creosote. Billet has also employed creosote irrigations in dysentery due to the *Entameba histolytica* of Schaudinn. He gives irrigations of from 1 pint to 1 quart ( $\frac{1}{2}$  to 1 liter) of 1 to 2 per cent. creosote, which has been previously mixed with oil of sweet almonds, in water. Usually two enemas a day are given. In most patients thus treated, the pain is rapidly relieved and the blood and fetor disappear from the stools. G. Zanardini (Semaine méd., xxvi, 462, 1906).

Though less frequently indicated than in amebic dysentery, it is the chronic type of the bacillary form in which an **appendicostomy** and subsequent **intestinal lavage** through the stump promises beneficent results.

The writer was much gratified with the results of treatment with **ippecac** given with a few drops of **opium** and **peppermint**, supplemented by **high rectal injections** of about 250 c.c. ( $\frac{1}{2}$  pint) of a solution of 5 Gm. ( $\frac{1}{4}$  drams) of **iodoform** in 1000 Gm. ( $3\frac{1}{2}$  ounces) of **mucilage of gum arabic**, introduced in the knee-elbow position under high pressure, with an attempt afterward to massage it up into the colon. The iodoform is left in the intestines for about ten minutes and the larger part is then washed out with two enemas of water. If the amebæ are ensconced in the appendix it may be necessary to remove that structure. Meyer (Deut. med. Woch., xxxii, Nu. 33, 1906).

In the treatment of chronic dysentery **appendicostomy** should be given preference over cecostomy unless there is some obstacle to its performance. The writer treated 31 cases of chronic amebic dysentery, chronic colitis, following acute dysentery. The oldest case had existed eleven years. Appendicostomy followed by irrigations gave satisfactory improvement in the symptoms, but did not suffice to produce cures. In the amebic cases the parasites rapidly disappeared. In 5 cases cecostomy was performed. The openings must not be allowed to close or the dysentery returns. Weakening of the abdominal walls with the formation of ventral hernia occurred in 8 (25 per cent.) of the cases. W. D. Webb (The Post-Graduate, Aug., 1910).

### AMEBIC DYSENTERY.

Amebic dysentery, or **amebiasis**, as it is also called, is an acute or chronic, ulcerative disease of the colon due to the *Entameba histolytica*, with a special tendency to the production of abscess of the liver, usually large and single; less often, small, multiple abscesses.

It has become evident that amebic infection is a systemic disorder, which may affect the entire body, and which, like malaria, syphilis, etc., is essentially a chronic condition. Charpin (Marseille méd., June 15, 1921) calls attention to various *atypical*

*forms*: (1) *Gastric* type, with anorexia, pain after meals, regurgitation, vomiting, and usually pain in the left iliac fossa. (2) *Diarrheal* type, with frequent stools. (3) *Appendiceal* type, with indefinite gastrointestinal symptoms and pain in the right iliac fossa. (4) *Rectal* type, with perineal discomfort. (5) *Pseudotuberculous* type, easily mistaken for tuberculosis.

**SYMPTOMS.**—The disease manifests itself in an acute and chronic form.

**Acute Type.**—In this variety the onset is sudden and sharp and the course acute. Without an examination of the stools it would not be possible to differentiate it clinically from bacillary dysentery. This may be the explanation of the statement that acute amebic dysentery is a somewhat rare condition. The patient is more or less abruptly seized with abdominal pain—*tormina* and *tenesmus*. The degree of *tenesmus* and frequency of stools are directly proportionate. The stools are bloody or blood-streaked mucus is passed, and in a few days they become copious, watery, of a dirty brownish-red color, and contain flocculi or shreds of tissue; they often have an intensely fetid odor due to the gangrenous sloughs therein.

G. C. Kilpatrick (So. Med. Jour., Apr., 1922) points out that infection by *E. dysenteriae* causes an extraordinarily small percentage of dysenteric symptoms as compared to the number of persons harboring the parasite. He considers the best stain for the detection of cysts the Donaldson iodine-eosin stain. Scalas (Rif. med., Jan. 29, 1921) found it feasible to distinguish amebic from bacillary dysentery with a *complement fixation test*, using an antigen from scraps of intestinal mucosa in the patient's stools. Le Noir and De Fossey (Bull. Soc. méd. des hôp. de Paris, July 6, 1922) facilitate the diagnosis of amebic dysentery by giving the patient 3 keratin-coated capsules, each containing 0.2 Gm. (3 grains) of *bile extract*,

3 times a day at mealtime. The dose is increased daily by 3 capsules until diarrhea occurs. The bile favors development of the amebæ.

Rapid loss of flesh and strength occurs; indeed, it is seldom that such extreme emaciation occurs as is noted in many of these acute amebic dysenteric cases. The heart becomes increasingly feeble, weak, and rapid; the temperature for the first few days ranges from 99° F. to 102° F. or 103° F. (38.9° C. or 39.4° C.), but often falls even below normal toward the end, and death may result from exhaustion within a week, or a copious hemorrhage from the bowels or perforative peritonitis may cause death. Many patients recover however, and some pass into the chronic form. Among those who survive, diarrheal disorders are common and occasionally cicatricial contraction of the bowel and final obstruction may occur.

**Chronic Type.**—In most cases the disease runs a more or less chronic course, in which the chief characteristic is attacks of alternating constipation and diarrhea. During the diarrheal periods there may be a little fever, abdominal pain and tenesmus, with some mucus or bloody mucous stools. General nutrition is well preserved. The tongue is apt to be red, beefy, the appetite impaired, and little inclination toward effort of any kind is often noted.

The duration is variable, months to several years. Some of these chronic cases may be spoken of as masked or latent, for infected individuals may harbor amebæ for long periods without being conscious of it.

The writer reports cases of infection with *Entameba tetragena* which illustrate the production of cysts by

this organism, its intermittency, the absence of cysts during acute symptoms, and their presence in formed stools long after the subsidence of acute symptoms. Infection in man appears to be the result of contamination of food with a small amount of fecal matter containing a great many cysts, during the first day or two after passing.

The great importance of examining the stools of all convalescent and recovered patients with entamebic dysentery for cysts and thus detecting "carriers" is apparent, for it is the cyst that is the infecting agent and not the large trophozoite. S. T. Darling (Archives of Intern. Med., Jan., 1913).

The indisposition may be slight and not such as to direct attention to the intestinal tract, except abdominal pain be present. Liver abscess may develop insidiously, and one of the complications may be the first evidence of the serious state of the patient.

**COMPLICATIONS.**—The most frequent and one of the most serious complications is hepatic abscess. Rogers believes that it is preceded for a variable period by fever of intermittent or remittent type, sweats more or less marked, leucocytosis, and an enlarged and tender liver. If the hepatic enlargement is irregular, dome-shaped, the condition is more readily recognized, but quite often the liver is uniformly enlarged.

The ameba of dysentery, such as is seen in the stools, is only one phase of the evolution of the parasite. The pathogenic phase is an intracellular parasitism. The young protozoon penetrates into a liver cell; at that time it is reduced to a homogeneous nucleus. The nucleus of the liver cell enters into karyolysis, the protoplasm develops vacuoles and tends to disappear completely, the parasite gradually supplanting its

host entirely. Job and Hirtzmann (Bull. de la Soc. méd. des hôp., Oct. 11, 1918).

Hemorrhage, perforative peritonitis, or peritoneal adhesions, and displacement of abdominal organs may result. Other infectious diseases—as typhoid, malaria, tuberculosis—may be associated with amebic dysentery, or amebic and bacillary dysentery may occur in the same individual, or other intestinal parasites may be associated.

**DIAGNOSIS.**—The most important aid to diagnosis is the finding of amebæ in the stools. If these are actively motile, with well-marked pseudopodia and a scarcely demonstrable nucleus, the probability is one is dealing with an amebic infection; but as non-pathologic amebæ are not uncommon, in liquid stools especially, too much stress should not be laid

or without change in shape, especially if chills, fever, and sweats exist, an abscess of the liver has probably developed. The leucocyte count is of some value. Not over 10,000 to 15,000 white cells are found in the average case of uncomplicated amebic dysentery; when liver abscess occurs, the count goes up to 20,000 or 30,000.

*Cytologic diagnosis* is stressed by G. R. Callender (Milit. Surg., June, 1925) for the rapid differentiation of the dysenteries, permitting of the application of proper treatment without the delay entailed by bacteriologic methods. With only a microscope and slides, one relatively inexperienced can thus make a presumptive diagnosis which will be correct in 90 per cent. of cases. Very fresh material is examined unstained in thin film under a cover glass. Thin smears are then made, fixed in Schaudinn's fluid, stained with hematoxylin and eosin, and if entamebæ are found, also with iron hematoxylin. The differential features are tabulated thus:

EXUDATE	BACILLARY DYSENTERY	AMEBIC DYSENTERY
<i>Blood.</i>	Varying amounts.	Small amounts to actual hemorrhage.
<i>Polymorphoneutrophiles.</i>	About 90 per cent. of exudate. Many show nuclear degeneration (ringing). Cytoplasm frequently contains fat.	Few. Cytoplasm of some of those present shows degenerative changes and in such the nuclei may appear pyknotic.
<i>Endothelial macrophages.</i>	Present in varying numbers. Actively phagocytic; frequently contain erythrocytes and leucocytes. Undergo toxic degeneration; "ghost cells."	Not seen except in cases also having bacterial dysentery.
<i>Plasma cells.</i>	Present, relatively more abundant early.	Present in small numbers.
<i>Pyknotic bodies.</i>	Proportionately insignificant, but are found.	Constitute about 80 per cent. of cellular elements.
<i>E. histolytica trophozoite.</i>	Absent unless the 2 diseases are both present.	Present and must be found to make diagnosis.
<i>Amount of exudate, actual hemorrhage excluded.</i>	Massive. A large part of the stool.	Small.
<i>Bacterial content.</i>	Low.	Very high, usually.

solely on the finding of amebæ. The agglutinin test will rule out bacillary dysentery. In the tropics all cases of diarrhea, however slight, should be looked upon with suspicion until patient, careful examination removes the doubt. The outline of the liver should be mapped out frequently. If it undergoes any changes in size with

**ETIOLOGY.**—*Geographical Distribution.*—Prevalent throughout the tropics, amebic dysentery is especially common in Egypt; indeed, it is almost the only form of dysentery met with in that country. It is less common in other parts of the African continent, and in India, too, its frequency varies greatly in different parts. It is very

common in the Philippines. In the tropics it is constantly present and may even be said to exist in epidemic form at times. Of special interest, however, is the fact that it occurs sporadically in any part of the temperate zone, though but very few cases have ever been reported from England. It is common in the United States, especially in the Southern States at low altitudes, near the sea level. Osler stated that the cases of acute and chronic dysentery admitted to the Johns Hopkins Hospital had been almost exclusively amebic, and that of 182 cases up to the year 1908, 123 had come from the State of Maryland.

The many cases in troops from Britain, Australia, and New Zealand in the present war are men who have never had amebic dysentery before. Many of the cases succumb before reaching the base hospital, and those that survive have frequently reached the condition of "running dysentery." Ronald Ross (*Lancet*, Jan. 1, 1916).

There exists a very general impression that house flies are the chief agent of spread of amebic dysentery. A careful study of the incidence of amebic dysentery in various parts of Egypt during 2 years showed, however, that the house fly was relatively unimportant in this connection. The prime necessity for the spread of amebic dysentery is the presence of an abundance of moisture and a high degree of humidity. The infection is spread through the use of contaminated water for drinking and for washing food which is to be eaten uncooked. The water, in turn, is infected by contamination from human excreta. The elimination of carriers from all positions in which they come into contact with foods greatly reduces the incidence of amebic dysentery. Woodcock (*Brit. Med. Jour.*, Dec. 28, 1918).

What appears to be the third case of amebic dysentery originating in Canada

was observed by the writer. Such cases are not as rare as usually stated; with careful examination of the stools of persons suffering from mucous colitis the amebas would be encountered in as high a proportion of cases as in England or the United States. Bates (*Can. Med. Assoc. Jour.*, Oct., 1925).

*Seasonal Influences.*—For some unknown reason the incidence of the disease varies, so that even in the tropics in certain years bacillary dysentery may prevail, while in other years amebic dysentery will constitute the larger number of dysentery cases, and, of course, it is not an uncommon thing to find the two associated.

In the temperate zone the amebic form of dysentery is most apt to occur in its active manifestations during the warm months.

*Age.*—Probably owing to the greater opportunities for infection, it is much more common among young adults, and especially is this true where troops are stationed. Children readily become infected, but, as a rule, less severely than adults.

*Sex.*—Far more common in young adult males, both in the tropics and in the temperate zones. Of Osler's 182 cases at the Johns Hopkins Hospital, Fitcher stated that 171 were males. One reason for this, and that a very important one, is that women are more temperate in their habits and less apt to be exposed to the direct cause of the infection.

Exposure and fatigue increase one's susceptibility to amebic dysentery; this is the likely explanation for its frequency among troops.

*Race.*—The white race would seem to be more susceptible than the black, according to Osler, also more sus-



ceptible than the natives of the tropics, and the disease is more amenable to treatment in the latter. This may be more apparent than real, however, because long residence acclimatizes them, and possibly active infections overcome may increase the resistance of the native race. Certain it is that the Caucasians live under better sanitary conditions than the natives, yet gastrointestinal and hepatic congestions are the rule among the Caucasians in the tropics, and especially is this the case with those who use alcohol freely.

*The Direct Exciting Cause.*—The *amebæ* were first discovered in 1859 by Lambl, in the stools of a child suffering with "enteritis," but he did not consider them of pathogenic import. They were again noted some years later, both by Cunningham and Lewis, in the stools of cholera patients and even in the stools of apparently healthy individuals. The name, *Ameba coli*, was first conferred by Lösch, who in 1875 found the organism in the stools of a chronic dysenteric patient who, at necropsy, was found to have extensive ulceration of the colon. He claimed for them in part only an etiological relationship with dysentery. He described them minutely as to shape, size, and character of motility. He, too, found that they succumbed to the use of enemas consisting of a solution of **quinine**, of a strength of 1:5000. Lösch attempted to reproduce the disease in dogs. He injected fecal material containing *Ameba coli* in the rectums of 4 dogs. In 1 of them he found amebæ eight days later, and in another, which was killed on the eighteenth day, he found rectal swelling, injection, and slight ulceration. Later, many at-

tempts have been made by a number of observers to produce the disease in cats and dogs by means of rectal injections with fecal material, and the cat especially has been shown to be quite susceptible. Kruse and Pasquale retained the enema in the experimental animals by placing a stitch through the anal structures. To obviate much if not all of the bacterial infection resulting from injections of fecal material, they later used the necrotic material obtained from the liver abscesses of amebic dysenteric patients, and under both conditions obtained pathological changes mimicking those resulting from the disease in man, and they also found the *Ameba coli* in the bloody, mucous discharges from the bowel. Marchoux succeeded in producing the disease in a number of cats. Those which lived over fifteen days developed hepatic abscess, single as a rule, occasionally multiple. It was found that a temperature of 45° C. will destroy the ameba, but does not harm the bacteria. Material so treated when injected proved negative. Harris failed to produce the disease by injecting cultures of all recoverable flora from a case of amebic dysentery, but did succeed in inducing it in a puppy, by an injection of fecal material from the same source, containing amebæ. A liver abscess also resulted. This seems conclusive evidence that an ameba exists with pathogenic properties capable of causing both dysentery and hepatic abscess.

It is to Robert Koch, however, that we are indebted for our first definite knowledge of the parasitic properties of the organism. While investigating cholera in Egypt in 1883, he found

them in the deeper portions of ulcers in the intestines of several cases of dysentery, and because of their deep position he looked upon them as exercising a causal relationship. It was his influence which led Kartulis to study them. Kartulis found amebæ in the stools of over 500 cases of dysentery in Egypt, and he also found them in the necrotic contents and walls of liver abscesses complicating that disease. He observed, too, that their number was seemingly related to the severity of the attack. Later he reported other evidence of a similar nature, likewise his failure to find the *Ameba coli* in other cases of intestinal disease than amebic dysentery. Amebæ have been found in the feces of individuals having various diseases, as was noted above (cholera patients), and even in the stools of normal individuals.

Osler in 1890 was the first observer in the United States to report the finding of ameba in the stools and hepatic abscess of a case of amebic dysentery. The patient came from Panama. Since then many others have reported cases of amebic dysentery occurring in the United States, among them being Musser, Dock, Councilman and Lafleur, Simon, Boston, Harris, and Stengel. Dopter reported some cases of amebic dysentery occurring in soldiers who had not been out of the country (France), the disease developing after they occupied a room inhabited shortly before by infected individuals.

[The writer has seen a case of a somewhat similar nature,—a young man of 23 years of age who had lived in Philadelphia all his life except for a brief stay in one of the New England States. He resided in Philadelphia with a young man who had contracted amebic dysentery in the Philip-

pinæ, and who had been successfully operated upon for a liver abscess after an appendicostomy. I saw the patient in consultation as a case of suspected typhoid, but not being able to concur in that opinion, and finding a large liver, I suggested a dysenteric colitis and possibly a liver abscess. Some days later I saw him again, and advised an operation. This was done and the liver abscess drained. Culture made from the liver abscess was sterile, but the necrotic material contained amebæ. He gradually sank and died, as he had been ill over three months in all. W. EGBERT ROBERTSON.]

The finding of amebæ in the stools of normal individuals and of those ill with other conditions than dysentery, and the fact that rectal injections in animals sometimes failed to produce dysentery in them, led to the question whether the ameba was really pathogenic or whether more than one variety existed, one type being pathogenic, the other benign. Several observers had already reported the finding of amebæ which were larger than that described by Lösch as the *Ameba coli*, and presenting a different encysted form. Quineke and Roos were among the first who endeavored to show that variations doubtless exist. With one type they succeeded in inducing in cats both dysentery and liver abscess, while with amebæ from another source they failed absolutely. They also described an intermediate type which caused mild intestinal symptoms when injected *per rectum* into cats. This led them to name these three as follows: *Ameba coli*, retaining the name given by Lösch to that type inducing most severe results, *Ameba coli mitis*, to the intermediate variety, and *Ameba coli vulgaris* to that type devoid of pathogenicity. These latter they obtained from the stools of normal individuals after the administration of

Carlsbad salts, finding amebæ in 9 out of 24. Schulberg also found them in the liquid stools of 10 out of 20 normal individuals after the administration of salines, but failed to find them in the solid feces. Kruse and Pasquale also found them in their own dejections and in those of many other normal individuals. Calandruccio swallowed amebæ and, though he continued to find them in his stools for some days, no morbid condition resulted. This knowledge caused Councilman and Lafleur to classify amebæ as pathogenetic and non-pathogenetic; the former they called *Ameba dysentericæ*, the latter *Ameba coli*. The accepted classification of today, however, we owe to Schaudinn, who termed the benign type *Entameba coli*, and the pathogenetic variety *Entameba histolytica*. A third form, described by Viereck in 1907, also pathogenetic, and called by him the *Entameba tetragena*, was at first believed to be a separate and distinct entity. Craig at first subscribed to this view, as did Schaudinn, but in a recent communication ("The Identity of *Entameba histolytica* and *Entameba tetragena*," Jour. Amer. Med. Assoc., May 3, 1913) Craig states that in 3 cases of amebic dysentery from Panama and one from the Philippines he had "been able to observe every form of both *histolytica* and *tetragena*, so far as nuclear structure and reproduction goes, that have been described for either species, and, as double infection in these cases can be practically ruled out, I am forced to conclude that there is only one species of *entameba* present, and that all of the forms found belong to the life cycle of *Entameba histolytica*." The fact is as Wenyon states (Jour. London School of Tropical Med., 1912, ii, part i): "The common

pathogenic ameba of man is still *Entameba histolytica*; the life history is not that described by Schaudinn, but that described by Viereck." The normal method of reproduction of *Entameba histolytica* in the cystic stage of development is by the formation of cysts containing 4 daughter-nuclei according to Craig (*vide supra*), but why encystment occurs in some and not in others of the same species, and what conditions determine this, are unknown.

*Entameba coli* is a harmless commensal in the human intestine, while *Entameba histolytica* and *Entameba tetragena* are pathogenic species, capable of producing amebic dysentery in man. *Entameba histolytica* and *tetragena* are strictly parasitic species and have not been cultivated. All cultivated species belong to the genus *ameba*, and differ greatly in morphology and life cycle from the parasitic amebæ which belong to the genus *entameba*. It has not been proved that any of the amebæ that have been cultivated are pathogenic to man. C. F. Craig (Amer. Jour. Med. Sci., Jan., 1913).

Musgrave is of the opinion that amebæ may become pathogenic at any time, and cites in support of this view an experience of his in Manila. Among 300 persons studied he found 101 with amebæ in their stools, of whom 61 had dysentery, the remaining 40 being symptom free. Within two months 8 of these 40 died and amebic infection of the bowel was found in all 8, and within the next three months all of the remaining 32 had dysentery.

*Cultivation of the Ameba.*—The importance of culturing the ameba on artificial media was early recognized. Kartulis claimed to have succeeded in inoculating non-sterilized, alkaline straw infusions from dysenteric feces and from the necrotic material of

dysenteric hepatic abscesses. Incubated at 36° C. to 38° C. for about forty-eight hours, a pellicle forms on the surface, composed of amebæ and bacteria. The amebæ, at first small, gradually increase in size and assume pseudopodial progression. Kartulis described small, round, non-motile bodies within them which he regarded as spores. When sterile straw infusions were employed, Kruse and Pasquale were unable to duplicate Kartulis's work, though they succeeded with unsterilized straw infusions. Therefore they regard this particular ameba as saprophytic, which would seem to be borne out by the indifferent results following animal experimentation.

Celli and Fiocci, Beyerinck, Scharlinger, Cunningham, Grassi, and others have attempted cultivation both on solid and in liquid media, but without success so far as pathogenic amebæ are concerned. It seems very probable that symbiosis with some of the bacteria is necessary for the development of pathogenic amebæ. Although Musgrave and Clegg succeeded in plating out the ameba, they were unable to demonstrate further growth and multiplication without the presence of living bacteria. This is curious in view of their presence in the bacteria-free, necrotic contents of liver abscesses; yet we know, from experimental evidence at least, that if dejections from cases of amebic dysentery be heated to 45° C. the amebæ are destroyed but no harm is done to the bacteria, and that fecal material so treated may be injected with negative result, while injections of the unheated stool give rise both to dysentery and hepatic abscess. Thus, it is evident that the bacteria alone are not responsible. No one has succeeded in producing growth and multiplication of

the ameba in the absence of bacteria, and while it is not possible, at present at least, to state which germ or germs are necessary to symbiosis, saprophytic organisms, when injected with the amebæ, usually fail to give rise to disease processes, while typical results follow when pathogenic germs are simultaneously employed. After amebæ become encysted, Frosch was able to destroy the bacteria by using a 20 per cent. sodium hydroxide solution. The amebæ thus obtained in culture with the spirillum of cholera, according to Musgrave and Clegg, when injected into the liver of a monkey, gave rise to hepatic abscess in which both amebæ and cholera spirilli were found, but similar injections into a monkey immunized against cholera were without result.

[The work of Duval with leprosy may throw some light on this subject. Noting the intimate relation between cell and bacteria, he reasoned it out that the bacterial proteolysis of the cell undoubtedly set free amino-acids and that these substances were probably necessary to the growth of the organism. This he proved to be the case. A parallel state may exist in amebic infection. Saprophytes do not break down tissue; hence no result when injected with the ameba, while pathogenic germs do, thus explaining the symbiosis and resultant pathogenesis. W. EGBERT ROBERTSON.]

The pathogenicity of certain forms of amebæ, especially the *Entameba histolytica* of Schaudinn, is generally accepted for the following reasons:—

1. The more recent the attack of dysentery, the greater the number of amebæ present.

2. Their intimate relation to certain tissues, notably the colon, in which they penetrate into the deeper portions of the wall, and to the liver in abscess, in which they are to be found to the exclusion of other infective organisms.

3. The uniform anatomical picture produced as a result of their activity.

4. The similarity, to those occurring in the human, of symptoms and morbid lesions resulting from injection into the colon of experimental animals or when the infected material is fed by mouth to the animals.

*Morphology.*—The *Entameba histolytica* is round, oval, or sometimes pear-shaped at rest, but apt to be very irregular when actively in motion by throwing out one or more pseudopodia. It is unicellular, possessing a hyaline ectosarc which is best seen in the pseudopodia. These latter may jut out from any part of the organism and seem to drag the ameba along as the contents gradually flow into them. The endosarc is a granular inner portion and contains a rather small nucleus, poor in chromatin, and hard to recognize. There may be several nuclei and vacuoles, and erythrocytes, leucocytes, blood-pigment, bacteria, small starch grains and the like may be noted in them.

According to Chas. F. Craig, encystment only occurs under favorable conditions the nature of which are not definitely known, and quite frequently, therefore, no cysts can be demonstrated. He also states that the normal method of reproduction in the cystic stage of development is by the formation of cysts containing 4 daughter-nuclei. In the active stage it is probable that the mode of reproduction occurs by binary fission or by gemmation or budding, irregular in type. The organism varies in size within rather wide limits, from about 10 to 50 microns, the average being about 25 to 30 microns, while the nucleus is 5 or 6 microns in diameter. The *Entameba coli* is smaller, from 10 to 15 microns

on an average, possessing a well-defined nucleus because it is richer in chromatin. It is less active than the *Entameba histolytica*. It is claimed by many to be a normal inhabitant of the bowel, probably the small intestine, and may be demonstrated in liquid feces after a dose of salts. It is non-pathogenic, therefore.

*Modes of Infection by Entameba Histolytica.*—Owing to our failure to grow amebæ in pure culture, it is not possible to isolate, from any source, an ameba of pathogenic properties answering all the conditions necessary to justify one in regarding it as the *Entameba histolytica*. We do know that both soil and water, and especially cistern or tank water, contain numerous amebæ, but even in the tropics the majority of them must be saprophytic, or amebiasis would be far more common. Drinking-water and fruits and vegetables eaten raw or only slightly cooked, and contaminated through fecal material used as fertilizer, may prove a source of infection. It is possible that the encysted form, which can withstand drying for several weeks, may be transported by air-currents and thus both food and water may become infected. The fatal case previously referred to certainly contracted the disease by contact with his brother-in-law, who resided in the same house. Many opportunities are given through various domestic utensils, toilet, or soiled hands.

**MORBID ANATOMY.**—*The Intestines.*—Almost any portion of the large bowel may be involved, or the entire structure may rarely be attacked. Probably the cecum and ascending colon are most frequently diseased. In the most extensive forms the entire wall of the large intestine is thickened and prac-

tically ulcerated in continuity. Occasionally the appendix is ulcerated, the cecum as a rule, and perforation of cecum or rectum is a common cause of fatal peritonitis or extensive periproctitis. The lesion is sharply delimited at the ileocecal junction. The earliest evidence of infection consists of a swelling of the submucosa, cellular proliferation and edema, local or diffuse. The mucosa over these elevated areas undergoes necrosis and sloughs, but the opening is often minute and practically always much smaller than the area of infiltration. In this stage the gelatinous submucosa constitutes the floor of an irregular ulcer with elevated, undermined edges. Soon the submucosa sloughs and is cast off as may the muscularis beneath, so that any of these structures may constitute the base depending on the stage, or the thickened serosa may remain, denuded.

Many of the ulcers will be connected by sinuous tracts covered by more or less normal mucosa. In less acute cases the ulcers are not so ragged; they are paler and the bases are often pigmented. Microscopically it will be at once noted that the process is not a purulent one, polynuclear leucocytes being almost absent. It is the fixed connective-tissue cells which proliferate and break down. The lymphatics are dilated, the blood-vessels turgid or thrombosed, the epithelial cells of the mucosa in the immediate neighborhood of an ulcer being the seat of cloudy swelling, dehiscent, the tubular glands often distorted, sometimes cystic due to pressure retention. Amebæ will be found in the bases and edges of the ulcers, out along the fistulous tracts, in the lymphatics and blood-vessels and in the tubular glands. Schaudinn be-

lieved they effect entrance to the submucosa by way of Lieberkühn's crypts. In the chronic cases all stages of the ulcerative process may be found up to areas of complete cicatrization. Coils of large and small bowel may become adherent. Stricture of the bowel with dilatation above may result in some instances.

*The Liver.*—It is very likely that infection takes place by way of the portal radicles, though it is difficult to explain why the hepatic lesion is large and single as a rule, rather than small and multiple as in cases of pylephlebitis. The single abscess is usually situated in the right lobe, either near the dome or less commonly beneath the under-surface, near the colon. Multiple abscesses are small, superficial, scattered throughout the outer portions of the liver, though the still smaller, miliary abscess may be widely diffused as in pylephlebitis. In addition, more or less necrosis of liver tissue may be noted focally, probably bacterial in origin.

The hepatic abscesses do not contain pus, and cultures are almost uniformly sterile. The contents consist of a dirty-yellow or reddish, necrotic material, containing blood and fragments of liver tissue. The early focus is well defined, containing a spongy material with more or less dirty, blood- or bile-tinged fluid through it. Still older foci have irregular, necrotic walls or dense, reactive inflammatory walls well circumscribing them. About every necrotic focus, though less marked or absent about the rarer, very chronic abscesses, is a zone of hyperemia. Amebæ may be found in the contents of these abscesses, but as a rule they occupy a close relation to the wall, and may not appear in the

drainage discharge for several days after operation.

*The Lungs and Pleura.*—These become involved secondarily when a liver abscess breaks through the diaphragm, an abscess of the base of the lung resulting, usually the right one, which may later rupture into the pleura, a pyopneumothorax resulting, or an empyema when the liver abscess ruptures directly into the pleura.

Rarely an abscess may rupture through the diaphragm into the pericardium, or, from the liver directly into the stomach, bowel or peritoneum, or a large vessel may be eroded.

The writer has observed numerous cases of suprarenal insufficiency in patients suffering from dysentery and dysenteriform enteritis. He describes a hyperacute choleric variety, death ensuing very rapidly; an acute variety characterized by a chronic suprarenal syndrome, recovery taking place under opotherapeutic treatment, and a light variety characterized simply by asthenia and fatigue.

The great frequency of this last form in soldiers suffering from enteritis may be explained by the functional overwork of the suprarenal glands, the normal rôle of which is the destruction of toxins produced during muscular activity.

**Adrenalin** administered in these cases gave very good results. R. Oppenheim (Med. Press, Oct. 11, 1916).

Case of amebic dysentery which developed in successive "pushes," the second being much more serious than the first. The special feature of the case was the evident injury of the suprarenals, the weakness being extreme, with very low blood-pressure and white dermographism. The ameba evidently produces some toxin that makes its influence felt on the suprarenals in particular. The writers consider that **emetine**

should be begun early in amebic dysentery and continued long after the disappearance from the stools of the ameba and especially of its encysted forms. With suprarenal manifestations **epinephrin** is indicated, its action here being as pronounced as in microbic infections. La Rivière and Villerval (Paris Méd., Apr. 21, 1917).

**PROGNOSIS.**—Many recover under rest and appropriate treatment, but prognosis should at all times be guarded, even though the type of attack seems to be a mild one. The tendency to relapse is always present.

In Manila at the present time, if early recognized and properly treated, the patients rarely pass beyond the diarrheal stage, and many, even without treatment, never become dysenteric in the common acceptance of the term. The severe cases develop from these and from the latent ones and their characteristics are well known. Children and old people seem to manifest a decided natural immunity, but while in children the infection, when it does occur, usually is of a mild type and very amenable to treatment, the reverse is true of the aged. A striking peculiarity in both classes, as well as in Filipino natives, is the absence of liver abscess. The writer has not seen a case of this in 1000 clinical cases and 100 autopsies of natives of the Philippine Islands. The disease manifests itself in a much broader and more comprehensible clinical picture than that generally allotted to it. Waiting for actual dysenteric symptoms before making a diagnosis is responsible for a large percentage of the present mortality from this cause in Manila. Bloody stools may occur early, but usually are not seen until considerable damage has been done, and may be absent till near a fatal termination or recovery. Prompt treatment of every patient in whom motile amebæ are found, without waiting for clinical dysentery, is the safe course to fol-

low. W. E. Musgrave (Jour. Amer. Med. Assoc., Sept. 16, 1905).

**TREATMENT.**—**Rest in bed** in all acute phases of the malady, with **liquid diet**. In all other forms, diet may be given according to the tolerance of the patient, governed of course by the severity of the intestinal symptoms. For the abdominal pain, **cataplasms** or **stupes** may prove comforting, and if tenesmus is present **starch water and laudanum** ( $\frac{1}{2}$  pint—250 c.c.—and  $\frac{1}{2}$  dram—2 c.c.) or hypodermics of **morphine** are the only measures which afford relief. Bismuth preparations, salol, and the so-called intestinal antiseptics given by mouth are of no value. An occasional dose of **castor oil** or several doses of a **saline** may prove serviceable. Kartulis recommended repeated doses of **calomel**, gr.  $\frac{1}{2}$  to  $\frac{3}{4}$  (0.03 to 0.048 Gm.) every three hours for several days, claiming that the number of amebæ was greatly reduced thereby. The danger of salivation must not be overlooked, and the fact that calomel is prone to set up a good deal of rectal tenesmus or add to the existing discomfort or actual suffering must also be borne in mind.

Report on the action of various substances on pure cultures of the *Ameba dysenteria*. Boric acid, euca-lyptol, ichthyol, oil of cassia, and infusion of quassia have slight, if any, effect on the amebæ.

**Tannic acid** 1:100, **sulphate of copper** 1:2000, **permanganate of potassium** 1:4000 and **sulphate of quinine** 1:1000 have a distinct moderate deterrent effect on the growth of the amebæ and cholera spirilla within thirty minutes.

**Succinic peroxide acid** 1:1000, **potassium permanganate** 1:2000, **sulphate of quinine** 1:500, **nitrate of silver** 1:2000, **argyrol** 1:500, and **protargol** 1:500 exercise a very marked

deterrent effect on the growth of the cultures within thirty minutes, and in the case of the silver salts and the succinic peroxide acid the action is plainly due to the destruction or inhibition of the growth of the symbiotic cholera spirillum.

**Thymol**, 1:2500, applied for fifteen minutes has the unique effect of destroying the amebæ, while exercising only a moderate effect on the cholera spirilla. Thomas (Jour. Amer. Med. Assoc., Jan., 1906).

The following method, which has given brilliant results with rarely a fatality on the Isthmus, consists in what might be called the rest supportive treatment. The patient is put to bed, absolute **rest** is enjoined, a purely **milk diet** is administered, and when great tenesmus is present **warm saline irrigations** are given two or three times daily. A preliminary dose of **castor oil** is usually advisable. The only internal medication which is given is the **subnitrate of bismuth**, which is administered in somewhat heroic doses, from a dram to a dram and a half every three hours. In the milder cases improvement begins in from three to five days; in the severer cases, in from ten to fourteen days. The stools then lessen in number and become formed, and in a comparatively short time—from one to three weeks—from twelve to twenty-four hours are passed without a movement. The diet is then gradually increased and the bismuth lessened in dosage. Usually the proteins, meat and eggs, are the last to be added to the full dietary. In from one to four weeks, depending on the severity of the case, the patients are perfectly well. It is then well to give **tonics** and recommend a **change of air**. Deeks (Med. Record, Dec. 12, 1908).

The writer employed **benzyl benzoate** in 8 cases of endamebic dysentery uncomplicated by bacillary infection, and witnessed markedly good results in every case. The doses employed varied from 20 to 30 drops of the 20 per cent. alcoholic solution in



a little cold water, 3 times a day, after meals. Haughwout, Santin and Asurzano (Arch. of Int. Med., Oct. 15, 1919).

The writer treated with favorable results 46 cases of amebiasis with **stovarsol**, a synthetic arsenical discovered by Levaditi in 1922. Of the 46 patients 27 were kept under observation; 21 of these were well and free from parasites 3.8 months on an average; 5 relapsed after 3.8 months; 1 relapsed repeatedly within periods of from 3 to 7 days. Johns and Jamison (Jour. Am. Med. Assoc., June 30, 1925).

The two procedures which should be instituted as early as possible in every case and which undoubtedly offer the greatest measure of success are, first, the use of **ipecacuanha** by mouth, and, second, the more or less frequent administration of **enemas**. **Ipecacuanha** should be given in salol or keratin-coated pills to insure their passage through the stomach undissolved. Nausea and vomiting are far less liable to occur. The mode of administration is as follows: Nothing by mouth for several hours, then begin at bedtime with 1 to 1½ drams (4 to 6 Gm.) of **ipecacuanha**. Reduce the dose each night by 5 grains (0.3 Gm.) and continue down to a 10-grain (0.6 Gm.) dose, then repeat the procedure if amebæ are still found in the stools. Subsequently, doses of 20 to 30 grains (1.3 to 2 Gm.) should be given each night over a period of many weeks.

Fifteen cases of amebic dysentery treated with **ipecac**. Each case had a uniform and highly favorable result. In no case was there a suggestion of a recurrence of the dysenteric attacks since the discontinuance of the **ipecac**. The interval elapsing in these cases varied from six months to four years. The essential points in the treatment include absolute rest in bed for a

period of at least two weeks and a proper regulation and restriction of the diet. S. K. Simon (New Orleans Med. and Surg. Jour., Nov., 1912).

**Ipecac** in the treatment of amebic dysentery in Florida has practically supplanted all other measures. The method employed is that suggested by Dudley, of Manila, about two years ago, and is as follows: The patient is put on a **milk diet** and confined to **bed**; after 4 p.m., he takes neither food nor water for four hours, when he is given 30 grains (2 Gm.) of **ipecac** in six salol-coated pills, swallowing these with as little water as possible. The patient takes no food or water during the night; the next day he takes water and milk liberally until 4 o'clock, and after four hours' fast is given 25 grains (1.6 Gm.) of **ipecac**. The dose is reduced 5 grains (0.3 Gm.) daily until the 5-grain (0.3 Gm.) dose is reached. Patient is then put on light diet and a daily dose of 5 grains (0.3 Gm.) continued for a week or ten days. If the pills are properly prepared there is little or no nausea. This treatment has given excellent results. Wallace (So. Med. Jour., Nov., 1912).

The writers recommend **Ravaut's method**. Upon appearance of the diarrhea from bile administration, an intravenous injection of 0.3 Gm. of **neoarsphenamin** is first given. Next day the patient takes 3 tablespoonfuls of Ravaut's paste, made up of 100 Gm. (3½ ounces) each of **powdered charcoal**, **bismuth subnitrate**, **syrup**, and **glycerin**, and 4 Gm. (1 dram) of **powdered ipecac**. This paste is given on alternate days for the succeeding 12 days, while on the intervening days 2 capsules of **neoarsphenamin**, each of 0.05 Gm. (¾ grain), are taken, 1 at a meal. Rapid improvement results. In cases with rectal ulceration, **enemas of bismuth**, **neoarsphenamin**, and **mucilage** were added, with good results. Le Noir and De Forsey (Bull. Soc. méd. des hôp. de Paris, July 6, 1922).

Superior even to **ipecac** and in some degree assuming the position of a true specific is **emetine hydrochloride** (see

the article on EMETINE, this volume) an alkaloid of ipecac introduced by Leonard Rogers (British Medical Journal, June 22, 1912) in the treatment of amebic dysentery and hepatitis.

Vedder had previously shown that this substance, the principal alkaloid of ipecacuanha, has the power in high dilutions of destroying amebæ in broth cultures; Rogers confirmed this by testing the effect of emetine hydrochloride on *Entameba histolytica* in dysenteric stools. When mucus containing numerous active amebæ was placed in the alkaloidal solution, the pathogenic organism was immediately killed and materially altered in its microscopic appearances by a 1:10,000 solution, while after a few minutes it was rendered inactive and apparently killed by as weak a solution as 1:100,000. Administration of emetine hydrochloride hypodermically in a few cases of amebic dysentery yielded excellent results. It did not produce vomiting, even though in the same cases ipecacuanha given by mouth had done so; the alkaloidal salt was at first given in doses of  $\frac{1}{16}$  grain (0.01 Gm.), this being equal to 15 grains (1 Gm.) of ipecacuanha. In the later cases  $\frac{1}{8}$  grain (0.02 Gm.) and even  $\frac{1}{2}$  grain (0.03 Gm.) were given without producing any ill effects on the patient, though their action on the disease was magical. The **hydrobromide of emetine** might also be given, but it is not quite so soluble as the hydrochloride. An advantage of the method is that the drug can be given even when the administration of ipecacuanha by the mouth is impracticable.

The writers deem **intravenous injections of emetine**, as recently recommended by Petzetakis, to be justifiable in cases refractory to ordinary methods of treatment with emetine and

organic arsenicals, but believe a dosage of 0.02 Gm. ( $\frac{1}{2}$  grain) a day by this route should not be exceeded, nor 0.25 to 0.3 Gm. (4 to 5 grains) as the total in a course of treatment. Nausea, exhaustion, and later asthenia, multiple neuritis, etc., are apt to follow such injections. **Heart-tonics** and **adrenalin** may be given to remedy these effects. Bensaude, Cain and Rachet (Bull. Soc. méd. des hôp. de Paris, May 15, 1924).

As to enemas, they should be given slowly and as high as possible, the patient lying on the right side with hips elevated and head low; 3 quarts (liters) of a warm solution of **quinine** in strengths ranging from 1:5000 to 1:500 may be given once or twice daily, each to be retained for fifteen or twenty minutes unless the pain is too severe. An initial enema of even greater strength may be employed, up to  $\frac{1}{2}$  per cent. or even 1 per cent. of quinine. It usually gives rise to buzzing, nausea, and occasionally vomiting, sweating, and a great deal of pain, but all these symptoms rapidly abate. Harris recommended **peroxide of hydrogen**, 1 to 2 pints (500 to 1000 c.c.) diluted with 4 to 8 times the amount of water. **Eucalyptol** or corresponding doses of the gum in 1 per cent. to 4 per cent. strength was advocated by Ford. Tuttle recommended simply **enemas of ice-water**, and reported a number of cases of which cures resulted from its frequent use. If definite results do not promptly follow the above measures an **appendicostomy** should be performed, and **ice-water** or **quinine**, or these agents in alternation with **hydrogen peroxide** or **eucalyptol**, should be introduced through the appendicostomy opening and the bowel thoroughly irrigated twice daily.

As soon as a diagnosis of liver ab-

cess has been made, the abscess should be opened and drained and the cavity thoroughly washed out with **quinine** solution.

In chronic dysentery, **irrigation** of the **colon** through the vermiform appendix or an opening into the cecum has given good results.

**Appendicostomy** is indicated when the case is refractory to rectal irrigations. The writer met with marked success in 2 cases, using **quinine** or **saline solution** through fistula. The operation should be performed in two stages: First bring base of appendix against abdominal wall, stitching meso-appendix to peritoneum; forty-eight hours later, apply cocaine to appendix, snip off with scissors, and introduce No. 10 rubber catheter. Anders and Rodman (Jour. Amer. Med. Assoc., Feb. 12, 1910).

Case of amebic hepatitis with febrile cycle of 11 to 12 days cured with 0.04 ( $\frac{1}{25}$  grain) injections of **emetine hydrochloride**. Laporte and Roques (Bull. Soc. méd. des hôp. de Paris, Apr. 13, 1922).

On the basis of results obtained, the writer advocates intensive **emetine** treatment before resorting to surgical measures. Falzi (Policlinico, May 15, 1922).

**Chaparro amargosa**, used as a domestic remedy for many years among the inhabitants of Mexico and Southwest Texas, has been availed of to some extent by the medical profession, with favorable immediate results.

The name, **chaparro amargosa**, means "bitter bush." This is a shrub growing to a height of about 4 feet, and belonging to the family *Simarubaceæ*. The writer advocates the use of an infusion made by boiling samples from all parts of the bush (roots, top, branches, leaves and red berries) for 30 to 45 minutes. After the infusion has been strained, the patient drinks a glassful of it 4 times a day, and also once or twice daily takes by rectum as much as he can conveniently re-

tain 15 to 20 minutes. The exact strength of the infusion cannot be stated, but it should have the color of weak tea. It seems to be non-toxic. In all cases seen by the writer there was immediate response to this treatment, the diarrhea and amebæ disappearing on the second day. Relapses, however, have been very frequent. A. A. Goldsmith (Ill. Med. Jour., Feb., 1926).

**Prophylaxis**.—Müller (Münch. med. Woch., Jan. 2, 1917) found 165 carriers of typhoid, paratyphoid or dysentery among the 20,019 men examined in about two months. He urges re-examination at intervals of all men who have anything to do with the preparation or handling of the food. An indigestible meal, or exposure to cold and wet, is liable to bring on the disease in a previously healthy carrier.

H. H. Dale (Lancet, July 29, 1916) found repeatedly that the usual hypodermic emetine therapy of carriers produced but a temporary disappearance of cysts from the stools. The **double iodide of emetine and bismuth** is a salt from which the emetine is liberated only after reaching the alkaline intestinal fluids; 3 grains (0.2 Gm.) of it contain 1 grain (0.065 Gm.) of emetine, and are equivalent to 60 grains (4 Gm.) of ipecac. It produced striking results. In the majority of cases the cysts were promptly and permanently removed by this remedy.

As a result of a comprehensive study, C. Dobell (Editorial, Brit. Med. Jour., Jan. 27, 1917) concludes that the proportion of individuals still infected with *E. histolytica* among the convalescents from intestinal disorders reaching England from the Mediterranean area has been about 18 to 25 per cent.

The evidence obtained as to the **double iodide of emetine and bismuth** encourages the hope that rapid cure of most cases will result. Not less than 36 to 40 grains (2.4 to 2.6 Gm.) in daily doses of 3 or 4 grains (0.2 to 0.26 Gm.) must be given; even more may be necessary in individual cases. The drug may exceptionally succeed in removing an infection with *E. coli*.

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**DYSMENORRHEA.—DEFINITION.**—The term dysmenorrhea is ordinarily taken to mean severe or inordinate pain attending the menstrual flow. Such a definition is, however, actually incomplete, as there coexists in dysmenorrhea a great variety of general forms of suffering, to which due recognition should be given.

**SYMPTOMS.—General Symptoms.**—Along with the local manifestations there are observed, as the most pronounced systemic symptoms, extreme nervousness, severe headache—occipital or frontal,—mental depression or excitation, and sleeplessness. In addition, there may be evidences of gastrointestinal irritation, such as nausea, vomiting of varying severity, and occasionally, a serous diarrhea.

**Local Symptoms.**—A varying degree of discomfort is common to very many women during the menstrual period. M. P. Jacobi placed the proportion of women who suffer more or less at menstruation as 46 per cent. There is thus, therefore, some difficulty in stating precisely the intensity of distress which may be accepted as constituting dysmenorrhea. In general, this term may be regarded as applicable whenever the pain is sufficiently severe to require medication or incapacitate a woman partially or wholly during the period.

The pain of dysmenorrhea, then, may be described as moderate or severe. In some instances it is nearly intolerable. The suffering may be most pronounced during the flow, and occasionally occurs as a postmenstrual pain. More typically, however, it precedes the beginning of the flow by a few hours to a few days, and is relieved when the flow has become thoroughly established.

Generally the pain is sharp and cramp-like or spasmodic in character, but it may instead consist of a more or less constant ache. It varies in quality in a given individual. The location of the pain is usually the suprapubic region; it is likely to radiate, however, to the sacral and lumbar regions and the posterior aspects of the thighs. There is no direct relationship between the severity of the pain and the amount of blood issuing; in fact, dysmenorrhea is, as a rule, less frequently observed and less severe among women who have an abundant flow for several days than among those with a scanty or moderate flow continuing only a day or two.

**ETIOLOGY AND PATHOLOGY.**—Dysmenorrhea prevails particularly in the early period of menstrual life and among young unmarried women. Among the married, and especially among those who have borne children, it is, on the other hand, much less frequent. Healthy young girls, according to Forssner, suffer just as often, if not oftener, than those who are anemic. Furthermore, dysmenorrhea is more common in young women free of pathologic changes in the reproductive organs than where such changes exist. Disorders of these organs exhibit no special relation to the character or severity of menstrual pain. Thus, dysmenorrhea appears more frequently as a functional disturbance than as a disorder of organic origin.

Numerous classifications of dysmenorrhea have been proposed, but no unanimity of opinion has been achieved in favor of any one. A commonly described classification is that which recognizes as separate groups the essential, the obstructive or me-

chanical, the neuralgic, the ovarian, and the membranous forms of dysmenorrhea. This classification, however, is unsatisfactory, not being founded on a logical, scientific basis, but rather on habit or custom. Indeed, in most cases a combination of several of the above-mentioned varieties—aside from the membranous form—actually exists.

For practical purposes the writer prefers to divide painful menstruation into the dysmenorrhea of functional origin and that of organic origin,—although with this division there may be difficulty at times in ascribing cases definitely to a functional or an organic source.

**Functional Dysmenorrhea.**—This is the type existing where no gross lesion can be found in the pelvic organs. That dysmenorrhea is in most instances functional is a view which has met with increasing acceptance, although the orthodox obstruction theory still has its advocates.

Functional dysmenorrhea is usually met with in adolescents who have not had an opportunity, either from infection, the hazards of conception, or the violence of parturition, to develop uterine, tubal, or ovarian disease. Its very obduracy to treatment is suggestive of a functional source. Generally it is neurotic in origin, and is thus apt to be met with in women of the emotional, hypersensitive type. It is also sometimes known as neuralgic or nervous dysmenorrhea. That it seems more frequent in stout, robust individuals than in those of delicate physique bespeaks the possibility of an underlying endocrin disorder. Yet, sometimes it occurs in women of poor general health, especially those exhibiting anemia.

The functional nature of this group of cases seems further illustrated in that it does not preclude conception, as well as in the fact that frequently it disappears after marriage, particularly if the latter be attended by its natural sequels, pregnancy and parturition. The reason for these favorable effects on the symptom is as yet unknown, and it must be borne in mind that the functional neuroses, according to a growing general impression, may in many instances have an underlying pathologic basis. An assiduous search for such a foundation for the symptom is consequently in order before any case can be labelled as neurotic. Nevertheless, the writer does believe that dysmenorrhea is very often to be regarded as a manifestation of nervous imbalance or explosion.

According to H. Meyer, dysmenorrhea is a functional disturbance attended with spasmodic contraction of the uterus, the cause of which is, in turn, psychic, the psyche reacting upon the uterus by means of its natural tendency to contract. Psychoneurotic proclivities may thus be expected to predispose to dysmenorrhea, and the relief from the latter afforded by parturition or even the mere physical relationship of marriage is accounted for by the resulting distraction of the psyche from its previous undivided engrossment in the menstrual function. Blacker is disposed to recognize a form of dysmenorrhea attended with spasmodic rigidity of the sphincter about the internal os, accompanied by colicky uterine contraction, while Forssner states that out of a series of 153 cases seen by him, he found emotional factors responsible for the trouble in 88. Stoddart regards menstrual pain as nearly

always a manifestation of "anxiety hysteria," and asserts that hysterical symptoms almost always accompany it.

Report of 4 cases of dysmenorrhea which set in following psychic traumas, such as eviction, investigation by the police, etc. The dysmenorrhea generally persists longer than the other psychoneurotic manifestations. The treatment consists of **rest, atropine, and psychotherapy**. Edelberg and Galant (Münch. med. Woch., Feb. 20, 1925).

Clow maintains that the restraint customarily pursued in young girls during the menstrual periods is actually conducive to dysmenorrhea. Out of 1118 schoolgirls aged from eleven to twenty-five years, 30 per cent. were found, at the time of matriculation, to suffer from menstrual distress. It was universally assumed by these girls that menstrual pain was aggravated by exercise, but upon the actual adoption of moderate exercise and freedom from restraint at the periods the proportion of girls with menstrual distress fell to 7 per cent. The disproof of the preëxisting erroneous assumption was observed, indeed, to have an abiding favorable influence on the symptom.

Some cases of dysmenorrhea have been connected with the so-called "sexual spots" in the nasal mucous membrane, having been found relieved by cocaine applications to this membrane during the periods. Such cases are now regarded as neurotic or hysterical, and the effects of cocaine ascribed to suggestion, cocaineization of other points of the body often yielding similar results.

Form of dysmenorrhea dependent upon *helminthiasis* described. The author finds Couillaud's "tongue sign" a reliable indication of the presence

of worms (*ascaris* and *oxyuris*) in these cases; the enlarged fungiform papillæ show as red spots at the tip or margins of the tongue. The treatment consists of small **enemas of tepid salt water** and **santonin** and **calomel** by the mouth for 3 or 4 days. In some cases of oxyuriasis, **bismuth subcarbonate** was given internally. The dysmenorrhea disappears along with the helminthiasis. G. Léo (Bull. de l'Acad. de méd., Mar. 8, 1921).

**Organic Dysmenorrhea.**—For the most part, dysmenorrhea occurs in patients uncommonly free from morbid pelvic conditions. Nevertheless there are numerous forms of organic disease of the reproductive organs that may give rise to the symptom.

Holden has maintained that retrodisplacements of the uterus, pelvic inflammatory disease, and myomas are the cause of nearly nine-tenths of the cases of true organic dysmenorrhea, these three groups being held responsible for 41, 37, and 11 per cent., respectively, of such cases. According to this, abnormal position of the uterus would, in general, seem to be at the bottom of the menstrual distress. Eighty-six per cent. of nulliparous women with retrodisplacements, according to Holden, suffer from dysmenorrhea. On the other hand, of multiparous women with retrodisplacements, only 25 per cent. suffer from this symptom. The present general opinion is that the actual cause of the dysmenorrhea attending retrodisplacements is, not an obstruction to the uterine lumen, but the associated inflammatory states of the endometrium, the uterine wall, or both.

Inflammatory disease of the uterus, ovaries or Fallopian tubes is the apparent cause of menstrual distress in 31 per cent. of the cases of such disease, while of myoma patients, 20 per

cent. suffer similarly, with the tumors as the apparent cause. The submucous or interstitial types of myoma are the most likely to induce dysmenorrhea, which they may excite either by stimulating attempts at expulsion or through interference with uterine contraction. Chronic appendicitis has also been observed to induce inordinate menstrual pain.

Appendicular dysmenorrhea observed in 90 per cent. of the writer's cases of appendicitis in women. Appendicitis can often be differentiated from adnexitis through the presence of dysmenorrhea in women previously not troubled with it. Pain appears 2 or 3 days before the period and recurs on the first day of menstruation, most severely in the right ovary and region of the appendix, from which it extends down the leg. In oöphoritis the pain instead extends through the whole abdomen. Since, on operation, the appendix was not found adherent to the adnexa, the conclusion was reached that the menstrual congestion induces an exacerbation of the appendicitis. Castaño (*Prensa méd. Argent.*, Feb. 20, 1925).

Much attention has been given—in the past more than at the present time—to acute ante flexion of either the normal or the infantile type of uterus as a source of menstrual distress. The resulting dysmenorrhea has been ascribed to obstruction to the escape of menstrual blood on account of the angulation of the organ, and been referred to as an obstructive or mechanical type of dysmenorrhea. The obstruction may be further accentuated, it has been thought, by menstrual turgescence of the endometrium. Again, a chronic endometritis and metritis might be thought to be activated during menstruation and play a marked rôle in the production of the pain. In some cases of

“obstructive” dysmenorrhea, on the other hand, stenosis of the internal os or the cervical canal, or a so-called pinhole external os, have been regarded as causes of the symptom.

In the writer's belief, true obstructive dysmenorrhea is a rare occurrence. If uterine displacement caused actual obstruction, the symptom would be even more common than it is. Numerous observations have shown that menstrual pain may occur in the entire absence of a mechanical barrier and that it may be wholly absent even in pronounced mechanical obstruction (Novak). Irrespective of the degree of twisting, turning, or bending of the uterine body upon the cervix, it would seem a physical impossibility for the cervical canal to be reduced to a tube having a diameter less than that of a red or white blood cell. No reference in the literature to a cervical canal of *microscopic* size has been found by the writer. Hubert, in sections of cervixes, was never able to demonstrate a stenosis in the anatomic sense. Again, even with extreme angulation, either anteriorly or posteriorly, pain does not occur constantly with every menstrual period. A painful period frequently alternates with a period that is wholly painless in the same individual. This fact in itself would appear sufficient to invalidate the theory of obstruction as the main factor in a definite group of dysmenorrheas.

“Ovarian dysmenorrhea” is a term which has been applied to painful menstruation attributed to congestion of the ovaries. Pain preceding the menstrual flow has been regarded as of ovarian origin, while pain accompanying the flow has been thought to arise in the uterus. The former type of pain could be classed more

properly, it seems, with the cases due to definite inflammatory disease of the ovaries. In this connection it should be borne in mind, however, that even where there are gross lesions involving these organs, menstrual pain is conspicuously absent. Except in hypofunction of the ovaries, which is generally associated with polyglandular dysfunction, the writer is inclined to doubt whether ovarian dysmenorrhea ever occurs. Further, where dysfunction of several glands exists, it is difficult to say which gland or set of glands is inducing the pain.

Hitschman and Adler recognize 3 phases in the cycle of the uterine mucosa, regeneration, secretion, and desquamation. These can always be recognized in scrapings. Examination of the material obtained in 41 women curetted for dysmenorrhea showed in most cases acceleration of the regenerative process or delay in the phases, the result of disturbed ovarian function. Likewise, of 31 women curetted for sterility, the majority showed pathological changes ascribable to ovarian dysfunction, while in a few abortion, tuberculous endometritis, and other causes were recognized. The indication is thus for specific treatment of the ovary, and in particular for stimulative X-ray treatment of these glands with  $\frac{1}{6}$  or  $\frac{1}{4}$  of the castration dose or 10 to 20 per cent. of the erythema skin dose. N. Temesvary (Zent. f. Gyn., Apr. 19, 1924).

Probably the commonest local cause of dysmenorrhea is rudimentary development of the uterus, dependent upon endocrin imbalance.

Analyzing 100 cases of dysmenorrhea, the writer was led to recognize one large group of cases due to faulty hygiene, upbringing and surroundings. These are thin, anemic subjects, with weak abdominal muscles, absent ab-

dominal breathing, faulty posture, constipated and with visceroptosis or poor circulation. The uterus is often arrested in development and easily exhausted by expulsive work.

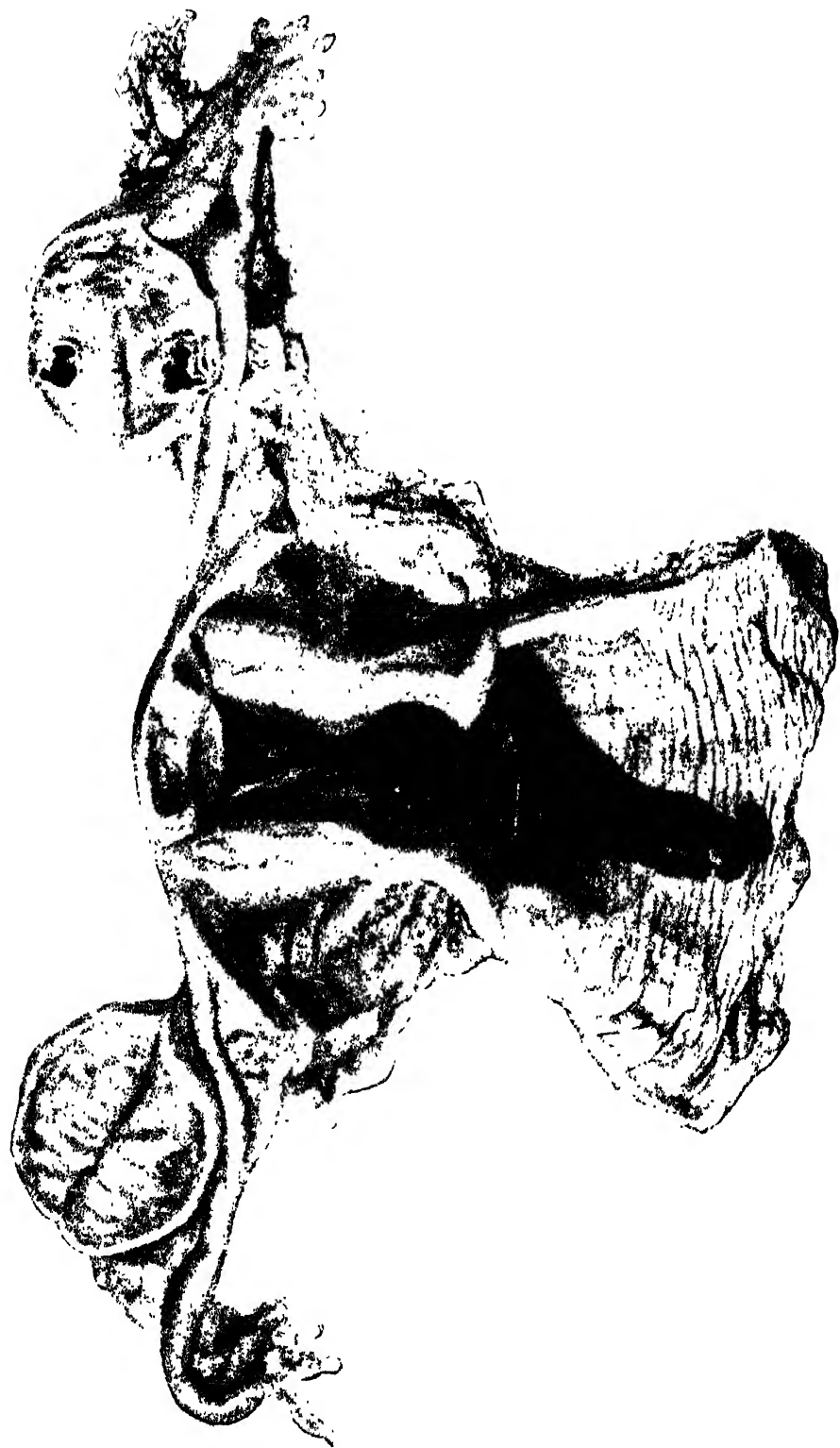
Another group is that in which the disturbance is functional and allied somewhat to migraine. Headache and nausea commonly accompany the menstrual pain. These are often sensitive, nervous, worried women with eye-strain and constipation, and the dysmenorrhea is one symptom of an "anxiety neurosis." Whenever the general symptoms are more marked than the local, general treatment is more likely to be successful.

In a third type, the symptoms and signs suggest some form of obstruction. While liquid blood may not be obstructed, clots, and especially solid, rolled up casts may cause considerable pain. The pain is intense and sudden, as in ureteral colic, and subsides rapidly when the clots are expelled.

The fourth and last type is that with complaint of pain in one iliac region either alone or before the central pain, with signs of arrested development of the genital organs. Leonard Phillips (Proc. Roy. Soc. of Med., Sept., 1923).

**Membranous Dysmenorrhea.**—By membranous or exfoliative dysmenorrhea is meant a form of pain accompanied by the expulsion of shreds or a partial or even complete cast of the endometrium. The shreds or pieces may be thin, or more thick if, as is rarely the case, there is a complete exfoliation. Sometimes pieces of membrane are mixed with blood-clot. Such a discharge rarely continues at the regular monthly periods, but may nevertheless occur several times in the same individual. The large pieces or casts may be mistaken for a discharge of decidual material following abortion, which they resemble macroscopically. Microscopic study, how-





Menstruating Uterus, Showing Corpus Rubrum in Left Ovary.



ever, reveals differences, the histologic make-up of the membrane being characteristic, while the cells are smaller than decidual cells and exhibit more irregularity, under separation, and more pronounced degenerative change.

This type of dysmenorrhea is met with usually in virgin or nulliparous patients. It has been attributed to inflammatory endometrial change due to gonorrhea or infection following abortion or the puerperium. As a matter of fact, however, most cases occur in women free of a history either of infection, abortion, or labor. The cause of the disorder must, therefore, be said to be unknown.

#### Intermenstrual Dysmenorrhea.

—This condition, also known as *periodic intermenstrual pain* or "*middle pains*," is not, strictly speaking, one of painful menstruation, since it is in no way associated with ordinary dysmenorrhea, and occurs quite independently of actual menstrual pain. It shows a time relationship to menstruation, however, in that the pain occurs with some regularity *between* the menstrual periods.

While this pain may be experienced at any time between the periods, it is most likely to occur halfway in the menstrual interval. Usually it continues for only two or three days, but it may persist longer, or even extend until the next menstruation sets in. It may recur only for a few months, or may continue for several years, or even from puberty until the menopause. The pain may be either dull or sharp, but is seldom of violent degree. It is felt usually in one or both ovarian regions.

This type of pain is met with most commonly in the active sexual period, but occurs more frequently in nulli-

para than in parous women. Out of 41 cases recorded by Kelly, 20 were between 20 and 35 years of age at the onset of the trouble, while 2 were over 35 years. Out of 66 cases mentioned by Heany, in the majority of which the pain had begun one or two years after puberty, only 3 of the women became pregnant.

Along with intermenstrual pain there generally exists some discharge. This was the case in 39 out of a total of 64 patients reported by Kelly. In most instances some lesion of the reproductive organs was found accounting for the discharge. The latter seldom contained blood, ranging in appearance nearly always from that of an ordinary leukorrhea to a yellowish or clear watery fluid.

Intermenstrual pain is associated in a majority of instances with adnexal inflammations. The ovaries, in particular, are frequently found to be cystic, hypoplastic, or the seat of hematoma. Occasionally, inflammatory tubal lesions exist, and sometimes intermenstrual pain of long standing has disappeared on removal of tubes the seat of hydrosalpinx or pyosalpinx. Sometimes, on the other hand, no pelvic lesion can be found. Such cases have been ascribed to sclerosis of the ovary, causing failure of mature Graafian follicles to rupture, the attendant tension being presumed to be a factor in producing the pain. This view presupposes that ovulation takes place regularly in the menstrual cycles, and such regularity has not been demonstrated to exist.

**PROGNOSIS.**—The prognosis in dysmenorrhea varies according to the conditions underlying it and the attendant ability or inability of the observer to utilize effective methods of treatment. In the minority of cases

in which dysmenorrhea is dependent upon definite lesions or defects, correction of these lesions or defects may be expected to yield a cure. Where such causative conditions cannot be found, the prognosis will depend in part upon the feasibility of improving the patient's general condition, marked betterment in this direction often influencing the dysmenorrhea favorably. Psychic influences may be similarly effective. While dysmenorrhea sometimes persists throughout the menstrual life, in many such instances it becomes gradually more tolerable. The prognosis where drug treatment alone is used is very uncertain, such treatment having generally only a temporary palliative effect.

In the membranous type of dysmenorrhea, spontaneous recovery sometimes occurs, while in other cases the symptoms recur regularly or irregularly for an indefinite time, in spite of all therapeutic attempts.

Intermenstrual pain is amenable to treatment, according to the results obtained in Kelly's series, in only one-half of the cases. Of the remaining one-half, some can be improved; others are uninfluenced by treatment.

**TREATMENT.**—In view of the varying factors that may be responsible for dysmenorrhea, as set forth under ETIOLOGY, it is obvious that the treatment must vary according to the indications existing in the individual case. A feature of the management which applies to all patients is the preliminary careful inquiry into the pathogenesis, to be followed, if feasible, by **removal of the cause**, whether by medication, operation, or both.

Further consideration of the treatment may, for convenience, be divided into the general and the local measures.

**A. GENERAL TREATMENT.**—In the majority of cases much more can be accomplished by directing treatment along systemic rather than on local pelvic lines. Among the most important general measures is **rest**, which may vary in duration from a few hours to a day or more, according to the severity of the pain. Rest between the periods, particularly an abundance of rest at night, is, however, of even much greater value than short rests during the period itself.

Especially in patients with functional neuroses or in poor systemic condition it is necessary to restore and maintain the general health at a high standard. The regular ingestion of three **generous meals** daily should be insisted on (most young girls are content with two). The patient should live in comfortable, well-ventilated rooms and secure an abundance of **fresh air**. Standing for long periods in a strained or awkward position must be avoided. Moderate **exercise** out-of-doors or under suitable indoor conditions will, however, be useful for "building-up" purposes and exert favorable effects on the nervous system and the gastrointestinal and pulmonary functions. Regular **bathing**, either at home or in bathing establishments, is likewise important.

Dysmenorrhea is in most cases curable by **exercise**. Operation should not be even suggested until **baths** and exercise, with judicious use of drugs, have been tried at least 6 months. The patients—and their mothers—are to be taught that the treatment of this symptom does not consist in subduing pain by drugs, but depends largely on health regulation by daily exercise in the open air, to be continued throughout the period. Having ascertained by examination that there is no evidence of disease or struc-

tural abnormality, the writer urges a bath at the beginning of the period, hot enough to flush the skin, and to be repeated daily throughout the period. Nothing gives relief so promptly. The daily exercise, which should involve bending and swaying movements of the body, should be begun some days before and continued throughout the period. If possible, it should take the form of work, games or sport, to divert the mind from the condition. For women doing sedentary work all day, exercise in the bedroom in the early morning will generally suffice, but in all cases it must be vigorous enough to promote a healthy glow or even sweating. In nervous women she generally prescribes a mild **analgesic** for the first 3 periods, but often finds it discarded after the first. A. E. S. Clow (Brit. Med. Jour., Sept. 27, 1924).

In view of the frequent coincidence of habitual constipation with menstrual pain, measures should be taken to obtain regular bowel evacuations, preferably by diet, habit, and exercise rather than the use of drugs. If anemia is present, it should similarly be combated with a generous diet and **blood reconstitutives**.

In the neurotic type especially, nervous excitement and emotions are to be avoided. In such cases much good can be done by **psychotherapy**. In various medical or surgical treatments for dysmenorrhea, indeed, suggestion is frequently an important factor in the benefit obtained. If, in certain cases, the symptom has been excited by suggestion, suggestion should, conversely, be effective in overcoming it. According to Stoddart, nearly every one of the large proportion of cases which he considers as being of the spasmodic hysterical types is amenable to psychotherapy.

No drug is specific in dysmenorrhea, and the agents of this class are, therefore, useful mainly for palliative rather than curative effects, although occasionally the organic extracts appear to exert some curative action.

In cases with extreme nervousness, sedatives such as the **bromides** are of service. Among the vegetable sedatives, **valerian**, **sumbul**, and **asafetida** have been used with asserted benefit. For the relief of the pain, **acetanilid** and **acetphenetidin**, while somewhat depressing, act best among the coal-tar analgesics. Either of these may be given in average doses, preferably combined with 1 grain (0.06 Gm.) of **caffeine**, repeated if necessary every two or three hours up to a maximum of three or four doses in the twenty-four hours.

**Benzyl benzoate**, advocated by Litzenberg, has been given in a 20 per cent. alcoholic solution in doses of 20 to 40 drops, repeated every three or four hours. To eliminate the unpleasant taste, it may instead be administered in 5-minim (0.3 c.c.) capsules. In the writer's experience with it in several obstinately violent cases, however, no relief was forthcoming, and he has discontinued its use.

Series of 80 unselected cases in which either **benzyl benzoate** or **benzyl succinate** was used. In the later cases the succinate was given, 2 five-grain (0.3 Gm.) tablets being ingested every hour until relief. Benefit was usually obtained within 3 doses, though a few took as many as 8. The results were good in 52, fair in 20, and poor in 8. J. J. Mundell (Surg., Gynec. and Obst., Nov., 1922).

Opium or its derivatives should never be used in dysmenorrhea, entailing too great a risk of habit forma-

tion. Similar considerations apply in the case of alcohol, which, while it cannot possibly do any permanent good, may do much permanent harm.

Definite utility can be accredited to **atropine** in the so-called "spasmodic" type of dysmenorrhea. According to E. Novak, it is especially useful in the cases attended with a scanty flow and sometimes with sterility. It diminishes the irritability of the autonomic nerve-terminals in the uterus. Ludwig and Lenz, by the use of a celluloid abdominal window in animals, witnessed complete relaxation of the non-pregnant uterus within a few minutes after intravenous injection of atropine sulphate.

This alkaloid may be administered in one of several ways: (a) Injection of 0.001 Gm. ( $\frac{1}{65}$  grain), dissolved in 1 c.c. (16 minims) of water, into the cervical canal, as advocated by Drenkhahn; (b) application to the cervical canal on a tampon saturated with a 1 per cent. solution; (c) hypodermic injection; (d) in suppositories; (e) by the mouth, in pills or capsules. The last-mentioned method—the easiest, especially in young virgins,—is commended by E. Novak, who administers  $\frac{1}{100}$  grain (0.0006 Gm.) three times daily, beginning two days before the expected flow and continuing until the second or third day of the flow. **Belladonna** by the mouth has also been used.

According to F. C. Coley, **pulsatilla** is a definitely effective agent, which will yield almost immediate relief in an attack and a permanent result after regular use at five or six periods. He found it especially useful in cases with pain for the first day or two of each period, or sometimes beginning a day or two before it, with the loss

usually small. He orders the following mixture to be started when the pain sets in:—

℞ *Tinctura pulsatilla*

(N. F.) ..... f3ss (15 c.c.).

*Spiritus chloroformi*. f3ij (7.5 c.c.).

*Aqua chloroformi* .. f3vj (180 c.c.).

M. Sig.: Two teaspoonfuls every 3 or 4 hours.

In certain cases showing a moderate degree of genital maldevelopment, **organotherapy** may be productive of some good, though if there is marked hypoplasia, no result is to be expected. The results are best in young patients—below twenty years. The following combination is suitable:—

℞ *Thyroidei*,

*Pituitarii* .....ãã gr. vj (0.4 Gm.).

*Gland. ovar. sicc.*

(whole) ..... 3iiss (10 Gm.).

Pone in caps. no. 1x.

Sig.: One capsule three times daily.

If organic drugs yield benefit, they may be continued for years or indefinitely. Where dysmenorrhea is associated with thyroid hypofunction, improvement, if not recovery, is apt to occur.

Out of 100 cases, 50 were treated by organotherapy. **Thyroid, corpus luteum, pituitary anterior lobe and mixed glands** were used separately and effectively. The majority received **hormotone**, 1 tablet *t. d. s.* for 7 days before and during the period. **Mist. cascarae comp.** (B. P.) was given daily throughout the month. If unrelieved, **analgesics** were used, sometimes with tincture of **belladonna** or **benzyl benzoate**, or at times **atropine sulphate**. Forty-six of the 50 cases were relieved at least sufficiently to work throughout the period in comparative comfort. Of 40 cases treated with antispasmodics alone, 34 were benefited. Ten cases were treated between the periods with **bromides** and **salicylates** combined with

**laxatives**, and during the periods received small nightly doses of **phenobarbital**; all were relieved. **Testicular extract**, alone or with **prostatic extract**, is sometimes successful in the type of cases with iliac as well as central pain and signs of arrested development of the genital organs. Leonard Phillips (Proc. Roy. Soc. of Med., Sept., 1923).

Endocrin disturbance resulting in vagotonia is the commonest cause of dysmenorrhea without gross pathological lesion in the pelvis. Where a deficiency of ovarian secretion is detected, **ovarian extract** in 5-grain (0.3 Gm.) doses 3 times a day, given continuously over a period of 2 or 3 months, is indicated. Ovarian extract is also of value in dysmenorrhea with hyperpituitarism, as well as in cases with an overactive thyroid, especially in the early stages with symptoms of mild hyperthyroidism. When the compensatory increase of the thyroid secretion has continued till there is exhaustion of the thyroid gland, the giving of  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.015 to 0.03 Gm.) of **thyroid** with the ovarian extract will give excellent results. Where the fault lies in the deficiency of either the thyroid or the pituitary, the exhibition of these glands is indicated. Where physical or mental shock or prolonged illness predisposes to the dysfunction, the patients usually show suprarenal exhaustion. Here **adrenalin**, followed by **strychnine**, has been found to give good results. A. Bercovitch (Canad. Med. Assoc. Jour., Apr., 1924).

**Applications of cocaine** in 10 to 20 per cent. solutions to the so-called "genital spots" on the inferior turbinates and nasal septum may prove of service in the rare instances of "nasal dysmenorrhea." Brettauer, reporting on 66 cases thus treated, asserted that over one-half of the patients were given immediate relief, with a permanent result in about one-third. The results thus seem equiva-

lent to those obtained with other therapeutic procedures, both medical and surgical.

**Marriage**, culminating in due time in parturition, constitutes the only wholly dependable recourse for the relief of obstinate dysmenorrhea, as has long been appreciated both by the laity and the profession. While not always available, this therapeutic measure, when resorted to, rarely meets with defeat, despite our lack of knowledge of its exact *modus operandi* in curing the symptom.

**B. LOCAL TREATMENT.**—In many instances, in the presence of the acute attack, a **hot water bag** over the suprapubic region, together with a few hours' rest on a couch or in bed, will bring relief. Sometimes, as an apparent paradox, an **ice-bag** is more effectual than local warmth.

In the intermenstrual intervals, systematic use of the **hot vaginal douche**, particularly in cases with pelvic congestion, will tend to prevent recurrence of the dysmenorrhea. Insertion of a **hygroscopic tampon** twice a week may be availed of in addition with advantage.

**Retrodisplacements**, if found, should, where operation is refused or inadvisable, be **corrected** and the proper position maintained by a vaginal **pessary**.

In obstinate dysmenorrhea the use of **radium** is preferable to radical surgical procedures, although in young women, particularly those who are anxious to have children, a prolonged exposure which would bring about permanent amenorrhea and sterility must be carefully avoided. In this treatment one of the radium salts is inserted, properly screened, into the uterine cavity. In young women especially, the dose should not ex-

ceed 300 milligram-hours. In older women, and particularly in those approaching the menopause, this limitation of dosage may be disregarded, and a dose sufficient to induce permanent amenorrhea seems desirable.

In the presence of chronic engorgement of the endometrium or uterine wall, or in acute antelexion of a normally developed uterus, **dilatation and curettement** may prove of benefit. In some cases added introduction of a



Fig. 1.—Conical cervix. Punctiform orifice. (S. Pozzi.)  
(Surgery, Gynecology and Obstetrics.)

**Surgical treatment** should be employed only where definite conditions calling for such treatment exist. In dysmenorrhea coexisting with rudimentary uterus or acute antelexion and ill development of this organ, surgical procedures are futile and contraindicated.

**stem drain** in the uterus may be useful, though at times such a foreign body proves irritating and harmful. In uncomplicated dysmenorrhea the results of simple dilatation and curettement will be found sufficient and compare favorably with those of more radical surgery of the cervix. Accord-



ing to Blacker, this procedure will permanently cure one-third of the patients and relieve an additional third for one or more periods. Rawls, in 117 cases, in some of which a pessary was used in addition, recorded im-

had been relieved, though in 7 per cent. the symptom had returned.

Blair Bell, an adherent of the obstruction theory of dysmenorrhea (in particular, obstruction at the internal os), maintains that the proportion of



Fig. 2.—Bilateral incision of the cervix. (S. Pozzi.)  
(Surgery, Gynecology and Obstetrics.)

provement in 77.8 per cent. and relief in 61.1 per cent., though the operation was attended by definite percentages of temporary and permanent morbidity. Holden, tracing 95 patients one to twelve years after dilatation and curettement, found that 40 per cent.

good results from dilatation and curettement is approximately doubled by the added performance of **cervical hysterotomy**, with or without **high divulsion**. For this combined procedure he claims cure in 86 per cent. of a large series of cases.

In severe essential dysmenorrhea, the writer firmly **packs the uterus and cervix** with **iodoform gauze** and leaves it undisturbed until the 8th day. If, as is usually the case, upon using a No. 10 or 11 **Hegar dilator** an unyielding band is found which precludes

Cleland (Amer. Jour. of Obst. and Gyn., Sept., 1924).

**Splitting the cervix**, anteriorly or posteriorly or both, following dilatation and curettement, has been frequently performed and may be product-

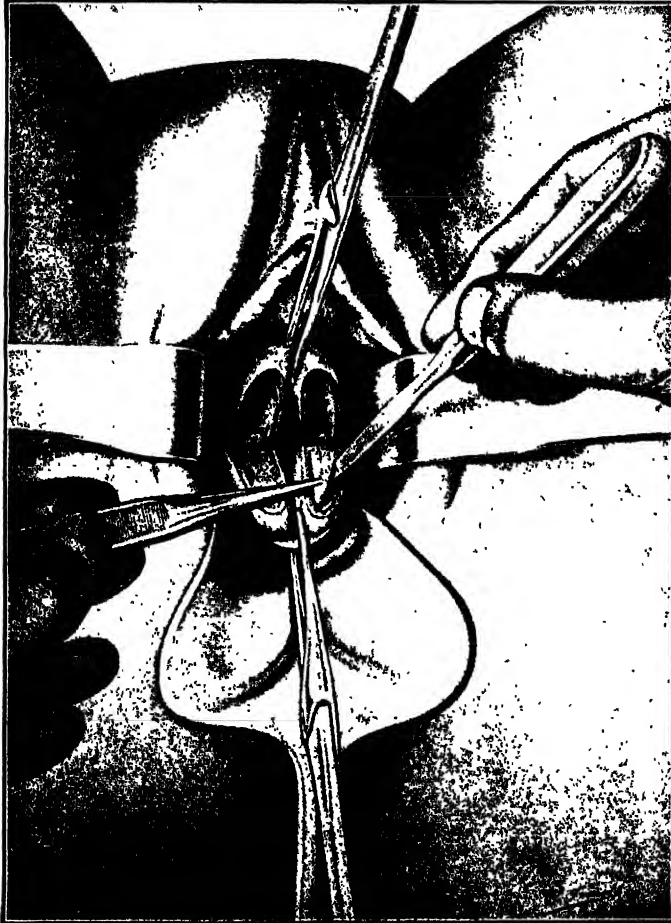


Fig. 3.—Hollowing out the cut surfaces of the cervix. (S. Pozzi.)  
(Surgery, Gynecology and Obstetrics.)

further dilatation, he makes, with a blunt-pointed bistoury, 2 lateral **incisions in the internal os** about  $\frac{1}{16}$  to  $\frac{1}{12}$  inch deep. Dilatation is then easily continued to a No. 14 or 15. Asepsis is imperative. Of 175 cases thus dealt with, 138 have been cured or markedly relieved, and in none have any ill-effects resulted. F. A.

ive of benefit. In the **Pozzi operation**, free bilateral incisions of the cervix are made and followed by excision of a small triangular piece of tissue from the middle of each of the four raw surfaces made by the incisions. The mucosa of the cervical lumen is then

sutured to the mucosa on the outer aspect of the cervix, thus closing the four raw surfaces and leaving the lumen of the cervix widely gaping. While this procedure has sometimes afforded relief it has the disadvantage

result of acute anteversion. In this procedure, after dilatation of the uterine canal, the posterior wall of the cervix is split to the cervicovaginal junction. Next, the angle of flexion of the uterus is incised with a scalpel

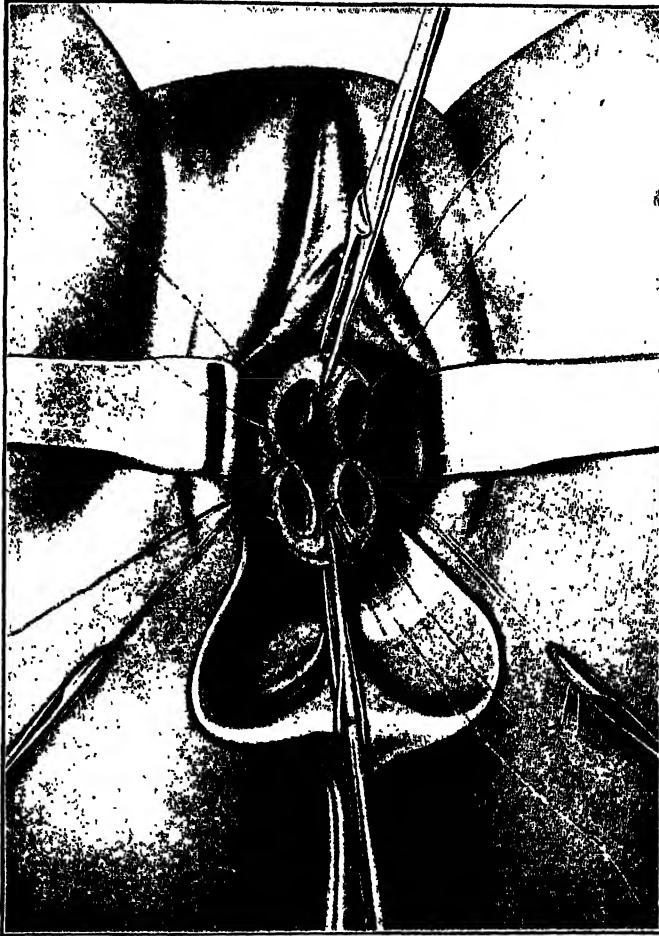


Fig. 4.—Introduction of the stitches. The commissural stitches are drawn tight. (S. Pozzi.) (Surgery, Gynecology and Obstetrics.)

of exposing the cervical mucosa to infection, with subsequent inflammatory changes and the dangers attendant thereto.

Preferable is E. C. Dudley's operation, which obviates the risk of exposure of the mucosa, and is of particular service in dysmenorrhea the

passed into the cervical canal. The mucomuscular layer of the uterus is incised widely enough to allow entrance of the index finger into the uterine cavity. From each side of the cervical raw surface a wedge-shaped piece of tissue is now excised. A cat-gut suture is introduced as shown in

Fig. 6, and two or three other sutures then introduced bilaterally to secure coaptation of the lateral surfaces. Finally, a superficial section of tissue is excised from the anterior lip of the cervix, and the resulting raw area

Dilatation of the cervix and light curettement of the uterus for the purpose of stimulation give a varying percentages of cures and relief in the hands of different surgeons, some reporting as high as 60 per cent. of cures, others, a much lower percent-

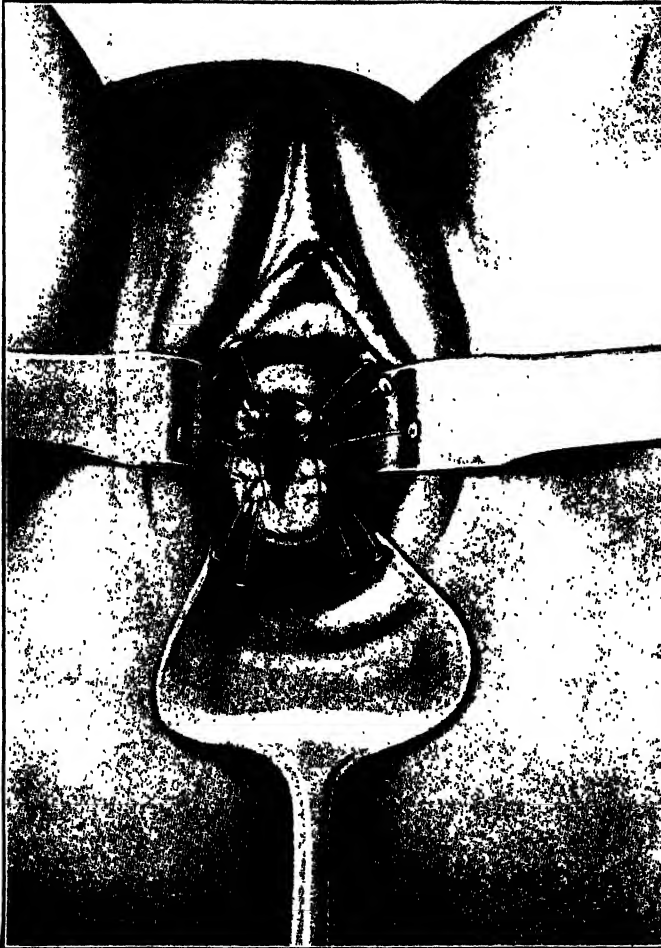


Fig. 5.—The operation finished. All the stitches have been drawn tight and the leaden guards applied. (S. Pozzi.)  
(Surgery, Gynecology and Obstetrics.)

closed by three or four sutures introduced transversely. While obviating exposure of the endocervix, this operation throws the cervix backward and high up into the posterior vaginal fornix, thus overcoming the angle of uterine flexion.

age. As regards the added use of a stem pessary, Crossen recommends the **Baldwin glass stem** or the **Dickinson hollow silver stem**, both of which, when properly placed, lie entirely within the cervix. Stacy and Joseph increase their percentage of relief an additional 13 per cent. by using the

Baldwin stem. The principal function of an added **uterine suspension** is to allow the uterus to receive its blood-supply properly and keep the canal free of stenosis. The author's experience, however, has been that where dilatation, curettement and suspension were done no relief was obtained until the **Dudley operation** was performed, while in cases where a Dudley operation was performed no relief obtained until a suspension was done. Dilatation and curettement alone are many times the means of stimulating the uterus of the married woman so that she may become pregnant, the pregnancy, in turn, curing the dysmenorrhea. C. C. Kennedy (Minn. Med., Aug., 1923).

In some instances, especially if there is an anteverted uterus in retro-position, intra-abdominal **shortening of the round ligaments** is helpful if added to dilatation and curettement.

Where there is clinical evidence of chronic appendiceal inflammation, **appendectomy** is sometimes followed by alleviation of dysmenorrhea.

**Treatment of Membranous Dysmenorrhea.**—This condition, when persistent, may be treated by means of the medical measures already described. In addition, several procedures are available for bringing on the menstrual period previous to development of the membrane. These comprise: **Thyroid gland** in small doses; **hot vaginal douches** twice daily for a week preceding the expected period, and **dilatation and curettement**, carried out four or five days previous to the period. **Calcium lactate** in 30-grain (2 Gm.) doses has proven serviceable, particularly where much bleeding attends the disturbance.

Case greatly bettered by 25 mgm. of **radium** element applied within the uterus for 8 hours. For women over 40, often with nervous systems wrecked

by a persistent dysmenorrhea resistant to all treatment, **hysterectomy** would seem to be the proper procedure. C. J. Miller (Amer. Jour. of Obst. and Gyn., Apr., 1925).

**Treatment of Intermenstrual Dysmenorrhea.**—In intermenstrual pain, when no local condition calling for operative correction can be found, treatment calculated to procure betterment of the general health, as by **rest, generous diet, bathing, and ex-**



Fig. 6.—Dudley's operation for acute anteversion of the uterus, showing method of splitting the cervix and introduction of sutures. (Bland, "Gynecology.")

**ercise**, should be applied. For the pain, **analgesics** may be given. As local measures, **external heat, hot douches, scarification, blood-letting, tampons and mechanical devices** may be used. **Dilatation and curettement** at times prove successful. Any **displacements** existing should be suitably corrected, and likewise, any **adnexal lesions**.

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## E

**EAR, DISEASES OF.** See EXTERNAL EAR, INTERNAL EAR, and MIDDLE EAR.

**ECHINOCOCCUS CYST.** See PARASITES, DISEASES DUE TO.

**ECLAMPSIA.** See PUERPERAL ECLAMPSIA.

**ECTOPIC GESTATION.** See ABORTION, TUBAL; also PREGNANCY.

**ECTROPION.** See EYELIDS.

**ECTHYMA.**—This disease constituted 30 per cent. of war dermatoses. Small pustules, scratched open and soiled with dirt, form scabs which do not end in healing. They may be very numerous.

**Treatment.**—After thorough cleansing, **potassium permanganate solution 1:4000**, **silver nitrate 5 per cent. solution**, and **tincture iodine**, are the best agents. The regular dressing should be **boric acid ointment** or **dermatol**. If the ulcers prove at all refractory the fine **Paquelin cautery** should be applied.

Warning against the use of wet dressings in this condition, where it affects the limbs, was given by Bodin (*Presse méd.*, Feb. 3, 1916), a French Army surgeon. Crusts having been removed from the ulcerations, these should be touched with a 1 per cent. solution of **silver nitrate**, dried with cotton, then dusted with **thymol iodide** or **subcarbonate of iron**. Around it a **zinc paste** containing **calomel** should be applied to prevent spreading of the infection. When superficial repair is slow, the silver nitrate stick may be used, and a **red cinnabar plaster**, extending beyond the ulcer only 1 or 2 mm., applied.

Chastanet (*Presse méd.*, May 11, 1916), in the ecthymatous sores observed commonly on the lower limbs of soldiers, first removed the crusts with sterile moist cotton pledgets, cauterized the lesion deeply with **silver nitrate**, and applied a sterile wet dressing. Cauterization was continued until the tissues became reddish, when, after a last cauterization of the entire lesion, including its margins, 1 in 10 tincture of **iodine** was freely applied. The sur-

face was then tamponed with slightly moistened cotton, and a dry sterile compress applied. If the lesion was not dry the next day, the procedure was repeated.

**ECZEMA (DERMATITIS).**—Within the last few years, a determined effort has been made to substitute the term Dermatitis for the term Eczema. That the latter term, for good and sufficient reasons, is rapidly outwearing its usefulness would appear to be a fact.

There is the greatest tendency, when a diagnosis of eczema is made, to allow matters to rest and make no attempt to search for a cause. This is due to the chaotic state of most minds concerning the etiology of this condition. Again, the term has been so vulgarized that, for the layman and not a few of those who should know better, all skin diseases are eczemas and consequently suitable for all remedies recommended as eczema cures. Furthermore, many conditions formerly grouped under the term eczema have been found to have a specific cause. In the new conception, eczema and dermatitis are identical, and the primary object in using the term dermatitis is to constantly remind the observer of the necessity of making every possible effort to determine the cause. Such a state of mind would undoubtedly tend to eliminate erroneous classification of many conditions as eczemas and at the same time hasten our acquisition of knowledge of all the real causes of eczema (dermatitis).

**DEFINITION.**—Eczema (dermatitis) is a catarrhal inflammation of the skin, particularly of the epidermis, characterized objectively by redness,

papules, variously sized vesicles, weeping, crusting and scaling alone, or a combination of two or more of these lesions. It is attended by a variable degree of thickening of the skin, the result of interstitial edema and cell infiltration. In its course it may be acute, subacute or chronic and is always due to two factors, namely a precipitating agent plus a special disposition of the skin without which it will not develop.

**VARIETIES.**—There are numerous objective varieties, mainly as a result of the frequent coexistence of two or more elementary lesions or of these lesions undergoing secondary change. The primary or elementary varieties are erythematous, papular and vesicular. As a rule, the secondary types rapidly develop from the elementary lesions. These are eczema rubrum, eczema squamosum, eczema impetiginosum or pustular eczema, eczema fissum, sclerosum and verrucosum. Nummular and infantile eczema are two special clinical types.

**SYMPTOMS.**—The *erythematous* type of eczema is most frequently seen upon the face, although it may make its appearance upon any other region or may be more or less general. It begins as a single hyperemic area, or several areas may appear simultaneously, usually upon one region. It may never go beyond this stage. The areas may be small or large, irregularly outlined, ill-defined, with swelling and even edema (*erysipeloid type*). There is more or less itching and burning. The eruption, as a rule, rapidly becomes marked, the parts reddened, somewhat thickened, and here and there a little scaly. There may also be, here and there (as a result of rubbing and scratching, or

spontaneously), a tendency to serous oozing. The affected skin is harsh, dry, and reddish or violaceous in color. It often persists in this form, and the skin may become considerably thickened and infiltrated. The swelling and edema which are often first present may subside, to a great extent at least, or these symptoms may reappear from time to time whenever there is an acute exacerbation. The parts may become quite scaly, and constitute a mild or well-marked scaly eczema: eczema squamosum. Occasionally, as a result of constant irritation, rubbing, and scratching, or from other causes, the parts become moist, markedly inflamed, with more or less crusting, constituting eczema rubrum.

The *papular* type of the disease, or *eczema papulosum*, presents itself as one or more aggregations of closely set papules, pinpoint to pinhead, or slightly larger, in size. The disease may also show itself as more or less discrete papules, with here and there aggregations. In color the lesions are bright or deep red or violaceous, often with a few vesicles or pustules interspersed. Itching is usually intense.

The extremities and the hands, especially about the joints, are the favorite sites. The course of this type is essentially chronic, some lesions disappearing and others appearing, and thus persisting for several months or indefinitely. In some instances, especially in some areas, the papules become so thickly crowded that a solid patch results, becoming more or less scaly—eczema squamosum. Or, at times, such a patch may develop into eczema rubrum.

The *vesicular* type of the disease

or *eczema vesiculosum*, may show itself on one or more regions, and consists of aggregated or closely crowded pinpoint- to pea- sized vesicles, with here and there discrete lesions, and at times with papules and pustules interspersed. It is usually a markedly inflammatory type, with considerable edema and swelling. Solid sheets of eruption may form. The vesicles usually rupture in the course of a few hours or days, new outbreaks occurring, or a raw, weeping, more or less crusted surface resulting. The oozing may be continuous or the process may decline, to remain quiescent or to break forth rapidly with repeated vesicular crops. Considerable thickening may take place and with the oozing and crusting make up a picture of the common clinical type: *eczema rubrum*. The face and scalp of infants, the neck, flexor surfaces, and fingers are the more common sites for the vesicular type. Its course is usually chronic, with several acute exacerbations, or, as already described, it may pass sooner or later into the common clinical type: *eczema rubrum*.

The *squamous* type of eczema, or *eczema squamosum*, is a clinical variety frequently met with, characterized by redness, infiltration, and more or less scaliness, with, especially when about the joints, more or less fissuring. The itching is variable, sometimes intense, and at other times slight. This variety is usually a development from the erythematous or papular types, and, like other types of the disease, is persistent and chronic.

*Eczema rubrum*, the oozing type of eczema, or somewhat dry, raw-looking type of eczema, usually results

from a pre-existing vesicular or pustular eczema. It is characterized by a deep red, weeping, oozing, raw-looking surface, with more or less infiltration of the cutaneous tissues. In some cases there is a combination of weeping raw surface with crusted areas. In other cases the weeping nature of the disease is a conspicuous feature, crusting scarcely having time to form: *eczema madidans*. Its most frequent sites are the face and scalp of children and the legs of adults; in the latter, in those especially advancing in years. In these cases of eczema of the lower legs varicose veins are often present as a precursory and concomitant condition. It is essentially chronic, showing little, if any, disposition to disappear spontaneously, although it may be somewhat variable. The degree of inflammation varies from time to time.

*Eczema impetiginosum* is not common. Its usual site is the scalp, especially in infants. It is really a pyogenic complication of eczema. Most commonly it begins as a form of the vesicular variety in which the vesicles are very closely set. There may be a mixture of vesicles and pustules. The symptomatology is the same as *eczema vesiculosum* except that the lesions contain pus instead of serum. More or less crusting is, as a rule, a conspicuous feature. It is commonest in the ill-nourished, the strumous and the unhygienic. This type is essentially chronic. It must not be confused with a true bacterial dermatitis.

The *fissured* type of eczema, or *eczema fissum* or *eczema rimosum*, is that type of eczema in which cracking or fissuring of the skin is the most conspicuous feature. It is common about the joints, especially about



the fingers, and in most cases is a part of an apparently slight erythematous eczema. Fissuring may occur in any type of the disease, especially when about the joints; but in most cases it is but slight in character. It is a persistent type of the disease, usually disappearing in part or more or less completely in warm weather. A somewhat analogous or allied variety of eczema is the so-called *crackled eczema*. This is usually a mild, subacute, erythematous eczema, involving large regions or the entire surface, numerous superficial cracks through the upper epiderm showing over the fissured surface.

*Eczema sclerosum* and *eczema verrucosum* are somewhat rare varieties of the disease. These types are usually seen about the ankles, lower leg, or feet. They commonly result from a pre-existing papular eczema. In many respects these types are analogous in their symptomatology: there is considerable thickening and board-like hardness, with, as a rule, much infiltration, but with the inflammatory element slight or comparatively so. The surface is rough, hard, and somewhat horny to the feel, and in the verrucous variety there is added to these several symptoms a variable degree of papillary hypertrophy, the surface having a distinctly warty appearance. Both types are essentially chronic and rebellious to treatment, demanding the strongest applications.

**Eczema Nummularis.**—This type of eczema is characterized by the presence of irregularly rounded coin-sized lesions which are circumscribed by a well defined border beyond which the skin has a perfectly healthy appearance. Early, the lesion is simply an erythematous spot whose surface

roughens while the patch itself thickens. Finally the roughened surface presents fully developed vesicles which tend to ooze. Fully developed, the lesion is red, thick, oozing, covered with vesicles in different stages of their development and crusts. The clearly defined border suggests a ringworm infection. The seats of predilection of this type are the wrists and backs of the hands. It is very rebellious and its disappearance is frequently followed by a rapid recurrence, almost always on the same spots.

**Infantile Eczema.**—The disease is common in infants and young children. It is unusual, comparatively speaking, in children past the age of 6. Even in those cases in which the disease begins in the first or second year and is persistent, it tends to decline spontaneously toward the age of 5 or 6, or even earlier, or, at least, at this period it will usually respond rapidly to any mild or indifferent application. The disease presents no special characteristics in the young, except that in the majority of such cases the inflammatory element is apt to be more marked. In by far the larger proportion of cases the face or the face and scalp is the seat of the disease; eczema of the region of the genitalia and anal cleft is also not infrequent.

All cases of infantile eczema will usually do well under treatment, although a disposition in many cases is shown toward relapse till the age of 4 to 6 is reached.

In eczema in infants and young children occurring about the legs and arms, usually as a vesicopapular or papular eruption, discrete and patchy, the disease is often obstinate,—much more so, as a rule, than in those cases

where the disease is limited to the face or face and scalp. The vesicular, vesicopapular, and moist or crusted inflammatory types—eczema rubrum—seem most frequent in the young.

**Regional Eczema.**—It is usual to describe eczema as it appears upon different regions, as, for instance, the hands, face, scrotum, legs, etc.; but the disease in reality differs little, certainly not materially, as it occurs upon different parts. The description of the several types of the disease as already given suffices.

It is noted that the most common seats for eczema in those of the active age, between 21 and 50, is about the hands; less frequently about the face or the scalp; the scrotum is not an uncommon site, and also the anal region.

In those past the age of 50 the most common site is the lower leg, although eczema of the face is not infrequently met with.

**GENERAL SYMPTOMATOLOGY.**—The subjective symptoms in eczema are itching, burning, and a sensation of heat. These may be severally present, or, as is more commonly the case, one is predominant. The degree varies, sometimes slight and at other times almost unbearable. As a rule, there are no constitutional symptoms, so-called, in eczema cases. In extensive general acute eczema there may be slight febrile action and sometimes slight chilliness at the outbreak of the attack. The degree of inflammatory actions varies in the same case from time to time and in different cases. The disease may be acute both in type and in course, running to an end in several weeks or one or two months. As a rule,

however, whatever the type of the inflammatory process—acute, subacute, or chronic—the disease is persistent and long continued, with, in most cases, little, if any, tendency to disappear spontaneously. Seasons often have an influence, the disease usually being less active or partly or completely disappearing in the summer weather. On the other hand, there are met with cases of the disease that are at their worst in summer time, and frequently disappear in the colder weather; such instances are, however, exceptional.

**ETIOLOGY.**—Eczema is a cutaneous reaction to many totally different causes all of which produce an analogous histological and clinical picture. In all instances this reaction is part of an inherent condition in the skin itself which we term predisposition. These causes are external in the larger number of instances and internal in the remainder, but both require a receptive skin.

Among the internal or constitutional influences which are or seem to be of some importance as active or predisposing factors are gout, chronic "rheumatism," gastrointestinal disorders of digestion or assimilation, dentition, loss of nervous tone, hypothyroidism and anaphylaxis. Anaphylaxis plays a large part, apparently, in the eczemas of children and in those whose attacks of eczema alternate with asthmatic attacks. The allergic skin tests for the determination of such sensitization are particularly indicated in such cases.

Gougerot has shown that eczema is the expression of a defensive reaction to some poison from within or without, the object of the edema being to dilute the toxic substances. Treatment should aim to reduce the

toxins, facilitate their elimination, compensate for deficient internal secretions by **organotherapy**, and in rebellious cases try to wash the blood free of toxins by **venesection** and **saline infusion**. Sabella (Policlinico, June 8, 1915).

The writer reports the case of a boy who, though apparently in good health, developed, when 4 years old, a more or less general eczematous eruption, in places dry and scaly, in others moist or weeping, accompanied by severe itching, which was worse at night. This eruption continued unabated notwithstanding much treatment, both local and dietetic, at the hands of pediatricists and dermatologists. Hypothyroidism was wholly responsible for the eczema, as shown by the remarkably prompt improvement following the administration of **thyroid extract** and the equally prompt relapse following its suspension. Edelman (N. Y. Med. Jour., Mar. 9, 1918).

Investigation to ascertain the rôle played by organisms in the causation of eczema. The method employed was to utilize the sensitization reaction of the skin following the intradermal injection of autogenous and heterogenous vaccine. The writer concludes that as the pyogenic organisms which are present in the lesions of eczema do not give rise to skin sensitization phenomena they are not the chief etiological factor in the causation of this disease. F. Walter (Derm. Woch., July, 1925).

The primary factor in chronic symmetrical eczema is usually some upset in the balance of the vegetative system. Two cases are described in detail to demonstrate that restoration of the vegetative balance should precede local measures, and may cure without them, merely by correction of auto-intoxication, abuse of alcohol or tobacco or treatment of congenital syphilis. Castex and Camauer (Prensa Médica Argentina, Oct. 10, 1925).

Immoderate habits in the use of certain foods, drinks, and drugs also indirectly or directly have an influ-

ence, such as alcoholic drinks, narcotics, and excess of tea or coffee.

Overwork, especially of a mental character, in those of hereditary eczematous tendency will often be provocative of an attack. That the hereditary disposition to the disease exists in many families is certain.

Among the external exciting factors may be mentioned cold and heat, especially the former; sharp, biting winds, and too liberal use of certain soaps; the handling of dyestuffs, chemical irritants, and the like; vaccination, and exposure to certain plants. Having the hands frequently in water, as with washerwomen, the handling of sugar and flour, and repeated antiseptic cleansing of the hands often bring about the various conditions of eczema of these parts known respectively under the names of *washerwomen's itch*, *bakers' itch*, *grocers' itch*, and *surgeon's eczema*.

There are 74 varieties of eczema associated with a corresponding number of callings. There is a "cement itch," a "bakers' itch," a "washerwomen's itch." Wool and cotton spinners have theirs, set up by irritating oils, which also cause eruptions in other occupations. The great majority of the lesions are naturally due to irritating chemicals of the most varied description in connection with the industrial arts. No less than 12 varieties of exotic wood are able to cause lesions in cabinet makers, turners, etc. Herxheimer (Deut. med. Woch., Jan. 4, 1912).

A special constitutional state is necessary for eczema for the following reasons: A combination of high butter fat, high sugar, orange juice and beef juice will produce an eczema in many children who never show the condition when normally fed. Eczema may be produced by many foods of widely varying types. Not every

child, however, will react to all of these foods. The one may respond to beef juice but will not tolerate milk; another will react to cane sugar but show no response to orange juice. The so-called exudative diathesis may be produced at will by the administration of certain food substances in a great majority of children. Kerley (N. Y. State Jour. Med., Nov., 1916).

A quarter of about 1200 persons who were eczematous had a healthy part of the skin brought into contact with certain substances for 24 hours. These were: formol, turpentine, quinine, sublimate, iodoform, tincture of arnica, leucoplast, and the leaves of the *Primula obconica*. B. Bloch (Zeit. f. klin. Med., xcix, p. 1, 1924).

The disease does not possess contagious properties, and in a disease so frequent as this, if such existed, they would have been clearly demonstrated.

In some cases of markedly inflammatory eczema, especially when of the pustular type, swelling of the neighboring lymphatic glands is noticed, but this rarely leads to suppurative change, the swelling and pain disappearing as soon as the inflammatory symptoms have abated. In some cases of eczema a condition of furunculosis is occasionally observed.

Case of chronic eczema of the cruro-genital region followed by fatal gangrene. Small superficial ulcers the size of a lentil developed over the sacrum and the temperature began to rise in the evenings to 101° or 102° F. (38.3° or 38.9° C.). Three days later the abdomen and thighs presented a remarkable appearance. The whole of the raw surface, which was now of a deep-red color, was picked out by clean-cut circular ulcerations the size of a lentil, which looked as though they had been deeply punched out of the skin. Each little ulcer was filled with yellowish pus and the whole surface was studded with these necrotic foci. In a day or

two adjoining ulcers began to coalesce, forming little troughs in the skin, while later on their bases dried up into blackish scabs, some of which toward the end were thrown off and replaced by granulation tissue. The general condition of the patient became very grave when the ulceration appeared, a typical septicemic temperature developed, and the pulse ran more and more rapidly and became feebler by degrees. The *Bacillus pyocyaneus* was found microscopically in enormous numbers in the exudation, and was recovered by cultures from the exudation, spleen, liver, and blood of the heart. C. H. Lancashire (Brit. Jour. of Dermat., July, 1910).

Case of hemorrhagic nephritis following impetiginous eczema in a girl, 10 years of age. Recovery took place in a short time. Halburstadt (Monats. f. Kinderheilk., Bd. x, Nu. 10, 1912).

#### PATHOLOGICAL ANATOMY.

—Eczema is essentially a catarrhal inflammation of the skin, and is seated chiefly in the rete and papillary layer; in long-continued and severe cases the lower part of the corium and even the subcutaneous tissue may be more or less involved, but never destructively. Hyperemia and exudation are to be found in all cases, either as punctate, localized, or more or less diffused conditions. The vascular changes are the same as those observed in all inflammations.

**DIAGNOSIS.**—There is no one lesion that particularly characterizes eczema. It is upon the appearance of the eruption as a whole that the clinical and not infrequently the etiological diagnosis is based. Eczema is to be distinguished chiefly from erysipelas, psoriasis, seborrhea, syphilis, scabies, and ringworm.

**Erysipelas.**—Markedly acute eczema about the face sometimes presents early in the course of the attack

a resemblance to erysipelas, but in the latter disease the border is sharply defined and elevated; it usually starts from one point and spreads rapidly, and is accompanied by systemic symptoms of more or less violence.

**Psoriasis** as commonly met with is not difficult to differentiate. The numerous, variously sized, sharply defined scaly patches, of general distribution, of psoriasis make this disease sufficiently characteristic. The face and hands are rarely involved, or only to a slight extent, at least, in psoriasis, while these regions are favorite sites for eczema. The psoriatic eruption often is seen most markedly on the extensors of the arms and legs, especially about the elbows and knees; eczema is more common in the flexures. Psoriasis is usually markedly scaly, eczema rarely so. In occasional instances, psoriasis is limited to the scalp, appearing here as several or numerous, variously sized, scaly areas, resembling squamous eczema of this part. The same differential characters can be here recognized, if the case is studied, as when seated upon other parts. Moreover, a careful examination will usually disclose the presence of several small or moderately sized characteristic psoriatic patches on the limbs, especially about the elbows and knees. Eczema of the scaly type is usually seated upon one region, is rarely generalized in its distribution, and the area or areas are rarely sharply defined. Itching is the rule in eczema and is often absent or slight in psoriasis. In many cases of chronic scaly eczema there is often a history of gummy oozing, but not in psoriasis.

The eruption produced as a result of the parasitic diseases, **scabies** and

**pediculosis**, is essentially eczematous in many of its characters, but is usually multiform, consisting of papules and pustules, the latter often being large in size. The distribution of the eruption in these parasitic diseases will often be sufficiently characteristic, and suspicion may be confirmed by the finding of the pediculus in pediculosis or by the burrow in scabies.

**Seborrhea** at times bears a close resemblance to a mild eczema, more especially as it occurs on the scalp. The seborrheic disease is, however, rarely inflammatory, except accidentally so; the scales are greasy, and there is no infiltration or thickening.

**Sycosis**.—Eczema of the bearded face may be mistaken for sycosis, but this latter disease is essentially one of the hair-follicles—*folliculitis barbæ*—limited to the hairy region of the face, and is rarely itchy. Eczema, on the other hand, is seldom limited to this region, but extends on to the non-hairy parts of the face, is not follicular, and is very itchy.

**Ringworm** can scarcely be confused with eczema, as eczema is seldom sharply defined, rarely ring-shaped, but is diffused, with no tendency to clear up in the center. In cases of a doubtful character microscopic examination of the scales will be sure to differentiate.

Among other diseases that should not be confounded may be mentioned rosacea, erythema, urticaria, herpes zoster, lichen planus, lichen ruber, and impetigo contagiosa.

**PROGNOSIS**.—The course of eczema in general is extremely variable. Under proper treatment most eczemas yield readily. Untreated and poorly treated eczemas will persist for years

in the first case and in the latter will be prolonged indefinitely and become more extensive. Eczemas, the cause of which cannot be discovered, as well as eczemas the result of known causes but with the patient persisting in exposing himself to these, naturally tend to persist, and if they clear up, tend to recur. Irrespective of the duration of the eruption, eczema may be said to be benign, in the sense that it never leaves a scar *per se*.

During the course of treatment the disease may show slight relapses, but each succeeding one is usually noted to be of a milder and less obstinate character. Several factors should influence the prognosis: the extent involved, the duration, previous variability, the nature of the exciting and predisposing causes, and whether these can be readily managed, and, finally, and of great importance, the care and attention the patient gives to the carrying out of the treatment advised.

The mystery of the sudden deaths of children with eczema of the scalp and face is discussed by the writer. In one such case the autopsy revealed an unsuspected streptococcal focus in one lung, the action, at a distance, of these germs having induced slight endocarditis and pleural effusion. In another case, an infant with eczema exhibited attacks of heart weakness, possibly from a similar action of the germs on the heart muscle. Another child of eleven months was in his care for recurring eczema of the scalp and face. The child was brought to him, after two months' absence, on account of a new patch on the cheek, and he was impressed with the dull look in the eyes, but nothing abnormal could be detected in the lungs or heart. The cervical glands were swollen. A salve of ichthyol and zinc oxide was ordered. The child seemed unusually quiet, and was found dead the second morning. Staphylococci

were discovered in the cutaneous lesions and in the internal organs. In such instances, infection with the staphylococcus alone did not cause, by any means, such severe symptoms as when the staphylococcus infection was supplemented by a cutaneous lesion, such as a croton-oil blister. The heart seemed to suffer particularly in these cases. The researches reported emphasize the importance of careful oversight of the heart action in cases of extensive eczema. Possibly the blood-pressure might afford useful information. Karrer (Jahrb. fur Kinderheilk., Bd. lxii, Nu. 6, 1905).

**TREATMENT.**—The treatment of eczema is both external and internal, depending on the etiological factors with which it is concerned, although topical applications are rarely dispensed with. In many instances, external treatment alone suffices, either because in the one case the constitutional and in the other the external cause has already been removed. In the anaphylactic types, avoidance of the harmful substance and, if this is impossible, **desensitization injections** are indicated. There are no drugs which may be given orally and considered specifics for eczema. There are certain general or hygienic measures which should receive attention, particularly if the inflammation is in any degree extensive.

Among the many distressing conditions secondary to fecal stasis and angulation of the sigmoid is chronic, weeping eczema. From an experience of 8 cases of this obstinate skin lesion the writer finds that it can be cured promptly by treatment directed to the relief of the intestinal disturbance. This treatment consists in the use of daily **enemas**, mild **laxatives**, and a regulated **diet**. Through the sigmoidoscope the sigmoid should be inflated and elevated, and any ulcerations of its mucosa treated by direct applications. Under such treatment the "weeping" will stop within 2 days

and the eczema will be completely cured in two weeks. All local treatment of the eczema should be stopped except **hot water fomentations** where there is skin infection. W. H. Axtell (Northwest Med., Oct., 1916).

The **diet** should be plain, but nutritious, all fancy dishes being avoided as much as possible. It is frequently advisable in generalized inflammations to thoroughly cleanse the gastrointestinal tract and keep the patient on a **milk and rice** diet for from one to several days.

The writer found **diet** of rice, bread, butter, and water effective in acute generalized eczema. Bulkley (Med. Record, Jan. 28, 1911).

The writers found the blood uric acid above the maximum normal figure in 44 per cent. of a large series of eczema patients, and by means of a **diet** calculated to oppose this condition cured a number of previously refractory cases. Schanberg and H. Brown (Arch. of Derm. and Syph., Dec., 1923).

Pork and salted meats, veal, pastries, strong acids or acid fruits, gravies, cheese, sauces, condiments, etc., and the excessive drinking of tea or coffee are to be eschewed. Beer, wine, and spirits are also to be avoided.

**Outdoor life** is to be commended in suitable weather, and **exercise**, especially systematic in character, is of great value.

**Arsenic** seems at times of special value in chronic, sluggish, papular and erythematous types. Each case must be carefully studied, and the predisposing factor or factors, if possible, discovered, and the treatment suitable instituted. When the itching is so intense as to prevent sleep, recourse may be had to the **bromides, phenacetin, chloral, sul-**

**phonal, trional, and the like**; opiates are apt to cause aggravation, but at times are indicated.

The writer confirms Lebedew, who described favorable results in the treatment of eczema and other skin diseases by **intravenous injection** of 10 per cent. **sodium bromide** solution. C. Wolff (Derm. Wochen., Jan., 1925).

The writers used Lebedew's method in eczema. Some patients recovered after 3 injections of 10 c.c. (2½ drams) of a 10 per cent. **sodium bromide solution**; others required more, up to 15. No untoward effects were observed. Hubschmann (Casopis lekaruv ceskych, Feb. 14, 1925).

Among the tonics that are often of value may be mentioned **codliver oil, hypophosphites, quinine, nux vomica, the vegetable bitters, iron, arsenic, and manganese**. Arsenic should never be given in the acute type, or in any case in which the disease is of the spreading or active character. Among alkalies, especially useful in gouty and rheumatic cases, may be mentioned **sodium salicylate, potassium bicarbonate, sodium bicarbonate, and the lithium salts**.

Among alteratives that occasionally are resorted to may be mentioned **calomel, colchicum, arsenic, and potassium iodide**. In some cases rather free action of the kidneys is desirable, and recourse may usually be had to **potassium acetate, potassium citrate**, and, in exceptional cases of more or less general eczema, the oil of **copaiba**. Laxatives form a very important class in the treatment of this disease, as indigestion with more or less active constipation is often a striking symptom. The various **salines and aperient mineral waters, castor oil, cascara sagrada, rhubarb, aloë, and other vegetable cathartics** are useful.

**EXTERNAL TREATMENT.**—In many instances an eczema will remain localized and in some instances even disappear spontaneously if the patient has sufficient control over himself not to scratch or rub it. All eczemas are prolonged by such manipulations. In commencing the treatment, the mildest remedies are at first advisable in order gradually to determine the tolerance of the patient's skin to the remedies being used. Acutely inflamed surfaces are best relieved by sprays or lotions or frequently changed wet compresses, as of **boric acid solution**. They are almost invariably made worse by the application of ointments. Before the application of active remedies, all crusts should be removed.

When advising a person with irritable eczema of the hands as to cleansing, the writer tells him to avoid soap altogether and to get **oil of sweet almonds** or **olive oil**, preferably in a shaker of the kind used by barbers to sprinkle liquids on the hair, and, in a separate container, the **yolk of an egg**. A liberal quantity of the oil is to be poured into the palm and thoroughly but gently smoothed and worked into the skin of the hands; this done, a small portion of the yolk (the yolk of one egg will serve for from 20 to 30 cleansings) is added, and the 2 briskly worked into an emulsion. A few drops of water aid at this stage, producing a thin, creamy white to dark suspension. The parts, rinsed now with cool water, are left soft and clean, without visible oiliness when dried. Glaze (Arch. of Derm. and Syph., May, 1924).

In the acute and in many subacute cases cleansing agents should be employed as infrequently as circumstances will permit.

When acute, weeping, erythematous eczema occurs on the face there is usually much edema in the infraorbital

region, and the condition may at first be mistaken for erysipelas. Greasy applications are best avoided, and simple wet dressings with folds of butter muslin soaked in normal **saline solution**, the patient being preferably confined to his room, are most acceptable. The following **calamine lotion**, applied on lint, will relieve the irritation and smarting:—

*R.* *Zinci carb.* (impuri) 3ij (8 Gm.).  
*Zinci oxidi* ..... 3j (4 Gm.).  
*Glycerini* ..... 3ss (2 Gm.).  
*Liquoris calcis*, q. s.  
 ad ..... 3vj (180 Gm.).  
 M. ft. lotio.

Upon the extremities, **lead lotion** is often best; it may be combined with the calamine lotion in equal parts.

When the exudation has practically ceased, powders or ointments may be applied. Of the former the **oleopalmitate of zinc** [or *Zinci oleostearas*, N. F. III] is useful. This may be mixed with one-half its weight of powdered starch. The following zinc cream is also a good application in these cases:—

*R.* *Zinci oxidi* ..... 3j (30 Gm.).  
*Adipis lanae* ..... 5ij (8 Gm.).  
*Olei olivæ*,  
*Liquoris calcis*, ana  
 partes æquales, ad 3iv (120 Gm.).

Misce. G. Norman Meachen (Pract., May, 1912).

A 6 per cent. **calcium chloride ointment** is often effective after failure of all other measures, causing many of the crusts to drop off in 24 or 48 hours and the skin soon to resume its normal appearance. Lampronti (Rif. med., Feb. 26, 1923).

The writer found **animal charcoal** effective in a case of abdominal eczema due to a fistula of the small intestine. Grueter (Zent. f. Chir., June 16, 1923).

In eczema of the face washing with a solution of 12 minims (1 Gm.) of **lactic acid** and 1½ grains (0.1 Gm.) of **salicylic acid** in 3¼ ounces (100 c.c.) of water is recommended. Philippon (Deut. med. Woch., Mar. 27, 1925).

The so-called **interdigital eczema** is in reality a mycosis, as Kaufmann found. Sabouraud showed that a



large proportion of these eczemas are parasitic affections. He advises **drying the skin** between the toes and washing only with **diluted alcohol**. Pinkus (Med. Klinik, Sept. 25, 1925).

A remedial application should always be made immediately after washing has been employed. In cases of a chronic, scaly, markedly sluggish character, the use of **soap and water** is resorted to frequently and has often a therapeutic value; indeed, in some such cases **green soap**—*sapo mollis*, U. S. P., may be occasionally or frequently used with advantage.

Applications are to be made in eczema two or more times daily, and when possible the continuous application is to be advised.

In the selection of external remedies for a particular case common sense must be employed. In those cases in which the type of disease is acute or subacute mild remedies are to be used. In the milder erythematous variety dusting powders of **zinc oxide**, **talc**, **starch**, and **kaolin** are soothing and beneficial; they may be used alone or immediately following the application of one of the washes given below. The conjoint use of **black wash** or **boric acid lotion** with **oxide of zinc ointment** or any mild ointment may give beneficial results. Or the simple oxide of zinc ointment with 20 to 30 grains (1.3 to 2 Gm.) of **boric acid** or 3 to 5 grains (0.2 to 0.3 Gm.) of **carbolic acid** to the ounce (30 Gm.) may be used. A compound lotion of calamine and zinc oxide, like the following:—

℞ *Calamina*,  
*Zinci oxidi* ..... āā ʒiiss (6 Gm.).  
*Glycerini* ..... ℥x (0.6 c.c.).  
*Phenolis* ..... gr. xx (1.3 Gm.).  
*Aqua* ..... ʒvj (180 Gm.).

M.

is valuable, and may be daubed on the surface repeatedly or by means of linen or lint kept wet with it and closely applied to the diseased surfaces, or a **boric acid lotion** with 1 or 2 drams (4 or 8 Gm.) of **carbolic acid** to the pint (500 c.c.) will be found beneficial, and especially applicable if the diseased surface is large; or, boric acid (15 grains—1 Gm.—to the ounce—30 c.c.) may be added to the above calamine and zinc lotion. A so-called **salicylic acid paste**, with or without 5 to 10 grains (0.3 to 0.6 Gm.) of **carbolic acid** to the ounce (30 Gm.), is often of great advantage:—

℞ *Acidi salicylici* ..... gr. x (0.6 Gm.).  
*Amyli*,  
*Zinci oxidi* ..... āā ʒij (8 Gm.).  
*Petrolati* ..... ʒiv (16 Gm.).

M.

Pastes such as this are, however, not advisable on oozy surfaces. A compound **calamine ointment** may be used in some cases with great advantage:—

℞ *Calamina* ..... ʒj (4 Gm.).  
*Amyli* ..... ʒss (2 Gm.).  
*Acidi salicylici* ..... gr. x (0.6 Gm.).  
*Ung. zinci oxidi*, q.s. ad ʒj (30 Gm.).

M.

**Diachylon ointment**, if a well-made one is procurable, is often serviceable.

**Washed crude coal tar** is an excellent remedy in all forms of eczema, alone or in the following formula:—

℞ *Tar, crude (perfected)*,  
*Zinci oxidi* ..... āā ʒj (4 Gm.).  
 Mix thoroughly and add  
*Lasclina* ..... ʒj (30 Gm.).  
 (White).

In some cases of eczema in which the grade of inflammatory action is subacute, stronger applications may be resorted to, although even in this class of cases it is advisable to begin the treatment with the milder appli-

cations already named. These latter may finally, if necessary, be made stronger and more stimulating by the addition of **white precipitate**, **red precipitate**, **calomel**, **resorcin**, or **tar**. Of the **mercurials**, 5 to 30 grains (0.3 to 2 Gm.) to the ounce (30 Gm.) is the usual proportion called for; of **resorcin**, 5 to 20 grains (0.3 to 1.3 Gm.), and of **tar**,  $\frac{1}{2}$  to 2 drams (2 to 8 Gm.) of the tar ointment to the ounce (30 Gm.) of mild ointment. **Oil of cade** may also be used,  $\frac{1}{2}$  to 2 drams (2 to 8 c.c.) to the ounce (30 Gm.) of ointment. A tarry ointment such as the following may also prove useful in these cases:—

℞ *Liquor carbonis detergens* ..... 5ss-ij (2-8 Gm.).  
*Cerat. simp.*...q.s. ad ʒj (30 Gm.).

[*Liquor carbonis detergens* is made by mixing together 9 ounces (270 c.c.) of tincture of soap-bark and 4 ounces (120 Gm.) of coal tar, allowing it to digest for eight days and then filtering. HENRY W. STELWAGON.]

For chronic, dry or weeping eczema the Strausz ointment is highly commended by the writer. It consists of **dehydrated wool fat**, 80 parts; **white vaselin**, 4; **zinc oxide**, 10; **balsam of Peru**, 5; a little **menthol**, and gaseous **oxygen** incorporated by a special procedure in the ratio of 7 to 8 liters of the gas per pound of ointment. The oxygen is supposed to stimulate "secondary cutaneous breathing" and promote cure, which is usually rapid. A. Voigt (Berlin. klin. Woch., July 18, 1921).

In vesicular, serous and acute cases the writers recommend a solution of **ferrous sulphate**, 10 Gm. (2½ drams); distilled water, 100 c.c. (3½ ounces), and **sulphuric acid**, 2 drops. When this has been applied and has dried on, a solution made by boiling 100 Gm. of **nutgalls** in 200 c.c. (6¾ ounces) of water is applied. In the preparation of the second solution, the liquid is boiled down to one-half its original

volume and a little **salicylic acid** added to prevent mold. This treatment, which results in an ink-like combination locally, immediately dries up the vesicles, which do not continue to secrete as after silver nitrate. Veyrières and Ferreyrolles (Bull. méd., Jan. 28, 1922).

A **flavine-starch poultice** is advocated for acute eczema or dermatitis. In preparing it, 4 tablespoonfuls of rice starch are mixed with 10 grains (0.6 Gm.) of **acriflavine** and a little cold water, and 1 pint (500 c.c.) of boiling water then added, with constant stirring, until thickening occurs. When nearly cold the mixture is poured on dressing cloth to form a layer  $\frac{1}{2}$  inch thick, and when quite set, is covered with a single layer of gauze or butter muslin and applied. It is changed 3 or 4 times a day, the part being bathed at each change in a 1:1000 solution of acriflavine in 0.185 per cent. sodium chloride solution. J. F. Smith (Brit. Jour. of Derm. and Syph., May, 1922).

**Crude coal tar**, recommended by Brocq in 1908, was found very effective by the writer in both infantile eczema and that of adults. His formula calls for crude coal tar and **zinc oxide**, of each 1 part, and **vaselin**, 16 parts. The tar and zinc are combined slowly and very thoroughly before admixture with the vaselin. The ointment is applied twice daily; each time, the remains of the previous application must be wiped away thoroughly with sterile gauze soaked in olive oil. No bandage, soap or water is used. The areas treated must be kept out of the sun and must not be too large, because of the possibility of toxic absorption. The drug should not be used where there is actual pus or vesiculation. C. J. White (Ther. and Diet. Age, Feb., 1925).

**Aristol**, 5 to 20 or more grains (0.3 to 1.3 Gm.) to the ounce (30 Gm.) of ointment base, may also be commended. In some instances preliminary paintings for several days

with a saturated solution of **picric acid** have proved of advantage, the observer waiting for the films or scale thus formed to come up, next applying a mild ointment for a few days, and then resuming the picric acid painting; it should not be applied to a large surface.

In some instances applications of dressings of a more or less fixed character are of advantage, such as the gelatin dressing, tragacanth dressing, and acacia dressing.

#### Gelatin Dressing:—

<i>R</i> Gelatin .....	15 to 25 parts.
Zinc oxide .....	10 to 15 parts.
Glycerin .....	15 to 25 parts.
Water .....	50 parts.

To this may be added 2 parts of **ichthyol**.

This is heated over a water bath each time it is to be employed, a good coating painted on with a brush, and when partly dry—in one to five minutes—the parts wrapped with a gauze bandage. The whole dressing becomes dry and fixed, and may remain on from two to six days, and then soaked off, cleansed, and a new dressing reapplied. In some cases the larger quantity of gelatin and smaller quantity of glycerin may preferably be incorporated, and then the gelatin coating will dry more quickly and will form a sufficient dressing without the gauze bandage, although this latter seems to be of real advantage in keeping the gelatin from becoming soiled and from being rubbed off. If the gauze is not used a small quantity of a dusting powder may be applied over the gelatin.

The above is especially applicable in the treatment of eczema of the lower legs. Other drugs may be added, but certain medicaments exer-

cise an inhibitory influence on the setting of the gelatin, and if added should always be used with a dressing more rich in gelatin and with less glycerin and less water; such remedies are **resorcin**, **salicylic acid**, and **carbolic acid**. **White precipitate**, **sulphur**, and **acetanilide** may also be incorporated in such dressings.

**Tragacanth Dressing.**—Pick's tragacanth dressing—linimentum exsicicans—is also a useful fixed dressing in the cooler weather. It consists of

<i>R</i> Tragacanth .....	5 parts.
Glycerin .....	2 parts.
Boiling water .....	95 parts.

To this can be added 2 per cent. of **boric acid** or 2 per cent. of **carbolic acid**, and 5 to 10 per cent. of **zinc oxide** or **calamine**, or equal parts of both.

This is smeared in a thin coating over the diseased area and allowed to dry on, which usually requires several minutes. The parts can then be bandaged or be sprinkled with some indifferent dusting powder. It is a more simple dressing than the gelatin application, requires no preparation, but is, upon the whole, less useful. Other medicaments may be added in addition to those already named.

The best treatment for eczema labiorum or *chapped lips* is to apply nightly **camphor ice**. In treating chronic eczema of the hand, if the patient is not able to stop his occupation, **rubber gloves** may be worn.

For eczema of the lids or nails the writer prescribes:—

<i>R</i> <i>Acidi salicylici</i> .	gr. vij (0.45 Gm.).
<i>Hydrargyri oxid.</i>	
<i>flav.</i> .....	gr. ij (0.13 Gm.).
<i>Petrolati.</i> .....	ad 3j (30 Gm.).

M. et ft. ung. Sig.: Apply to part after washing off crusts with olive oil.

In eczema of the legs, where we have a retarded circulation, varicose veins, the

patient should elevate the legs if practicable or wear a bandage well applied. Applications of **silver nitrate** and dusting powder are useful; in stubborn cases **oil of cade** is indicated. S. Moskowitz (N. Y. Med. Jour., Feb. 13, 1909).

**Acacia Dressing.**—This constitutes another fixed dressing that is readily applied and which may be used on dry parts. A good formula is the following:—

℞ *Mucilage of acacia* ..... 5 or 6 parts.  
*Glycerin* ..... 1 part.  
*Zinc oxide* or *calamine*,  
 or a mixture of both.... 2 parts.

**Carbolic acid** or any other drug may also be added if desired.

This is painted on with a brush or smeared over in a thin layer with the finger; it dries in a few minutes. If at all sticky, or for further prevention against this, a dry powder of **zinc oxide** or **talcum** can be applied over it.

The writer recommends the application of the following ointment in cases of eczema of the face in children:—

℞ *Salicylic acid*,  
*Precipitated sulphur*,  
*Pulverized camphor* ..... 5 gr. xv (1 Gm.).  
*Oil of cade* ..... 5iiss (10 Gm.).  
*Zinc oxide* ..... 5v (20 Gm.).  
*Petrolatum* ..... 3j (30 Gm.).

M. et ft. unguentum. Rostaine (Revue des hôpitaux, No. 5, 1910).

In eczema of a chronic sluggish type strong applications must usually be made before a result is brought about. The different remedies and combinations referred to in speaking of the treatment of the subacute type may be first tried; later, when necessary, treatment may assume a bolder character, various remedies being used in stronger proportion. Of value

in many of these cases may be mentioned: Ointments of **calomel**, 40 to 80 grains (2.6 to 5.3 Gm.) to the ounce (30 Gm.); **white precipitate** of about the same strength; **salicylic acid** ointment, 20 to 60 grains (1.3 to 4 Gm.) to the ounce; **resorcin**, about the same proportion; **sulphur**, 10 to 60 grains (0.6 to 4 Gm.) to the ounce (used at first with caution); **tar ointment**, either in official strength or somewhat weakened, or the **liquor carbonis detergens**, with **simple cerate** or as a wash, pure or diluted.

In the seborrheic eczema of infants, improvement and cure usually follow the **change from pure milk diet to mixed diet at the end of the first year**.

The cure of eczema in infants depends upon changes in their diet. Reduction of milk is the principal point of managing these cases, and carbohydrate food must be given to make up the deficiency in the foodstuffs. After the fourth month this is very easy, as the child can be fed on various cereal preparations and also given fruit-juice. In later months the albumin of eggs must be avoided, as it is as badly borne as the milk proteins. Whey mixtures may be used in cases where the child is too young to take any food other than some form of milk. The whey may be modified with sugar and cereal gruel—a diet with which Finkelstein has had great success. Freer (Munch. med. Woch., Jan. 19, 1908).

An ointment of 20 to 40 grains (1.3 to 2.6 Gm.) of **pyrogallie acid** to the ounce may be cautiously tried in sluggish, thickened, obstinate cases of limited area. The same may be said with regard to **chrysarobin**; but this latter should not be used about the face. The various fixed dressings referred to in the treatment of the subacute variety will also be of value in the chronic type. **Collodion** may also be used as a basis for fixed dress-

ing in localized areas of disease. The stronger **salve-** and **plaster-mulls** and the **medicated rubber plaster**, the latter especially in the sclerous and verrucous forms, are also of distinct advantage in these cases; in sluggish, thickened areas repeated **shampooing with green soap and hot water**, rinsing off, and immediately followed by a mild ointment applied as a plaster, acts admirably in some instances. Painting such areas with a solution of **caustic potash**, 1 to 5 per cent. strength, allowing it to act for a few minutes, then rinsing off, and applying a mild ointment, is a somewhat similar method of treatment which is serviceable at times. In some obstinate cases, thoroughly stirring the skin with a strong remedy, instituting a substitutive inflammation, and then applying mild remedies will not infrequently bring about the desired result. Finally, in persistent cases recourse may be had to the use of the **X-ray**, which is useful in all forms of eczema, and particularly for the very itchy chronic lesions. It is our best anti-pruritic in these instances.

The writer successfully treated with the **quartz lamp** 12 cases of eczema of various types, which had resisted all other methods of treatment. It should be tried in obstinate, recurring vesicular eczemas which have failed to respond to other forms of treatment, including the X-rays; in pustular eczemas of the scalp and beard to prevent relapses; and in chronic eczemas with infiltration, of the psoriasiform type, for the removal of the infiltration. Rave (*Archiv f. Dermat. u. Syphilis*, Bd. ci, Heft 1, 1910).

The writer recommends **venesection plus saline infusion** in the treatment of skin diseases. This "lavage of the organism" washes out toxins. He withdraws 100 or 200 c.c. ( $3\frac{1}{2}$  to  $6\frac{1}{2}$  ounces) of blood from a vein and then infuses

without removing the cannula 300 or 700 c.c. (10 to  $23\frac{1}{4}$  ounces) of a 0.9 per cent. salt solution, repeating this from three to six times at intervals of five or six days. No by-effects to cause uneasiness were observed on the part of the kidneys or vascular system in any case, so that he does not hesitate to apply this treatment even to the elderly, up to the age of 73. No fever was observed, and the technique can thus be applied to out-patients. The best results were obtained in pruritus, urticaria, furunculosis and eczema. Simon (*Deut. med. Woch.*, Nov. 30, 1911).

The writer has the patient expose the part affected in the **heat** from an oven or other source at a temperature of 100° or 115° C. (212° or 239° F.), passing the part gently back and forth five or six times until the prickling from the heat has stopped, doing this two or three times and repeating it three times a day at first. The part should be held closer to the source of the heat each time, and the patients do this instinctively when they feel the relief from itching and the benefit generally from the process. After the dry exposure a folded towel is dipped in boiling water and laid gently on the part and moved to and fro, applying this with more force each time. Patience and perseverance were necessary to conquer the old chronic eczema in the case reported, the writer himself being the victim, but permanent success finally crowned his efforts after a number of relapses. Toth (*Jour. Amer. Med. Assoc.*, from *Berl. klin. Woch.*, Oct. 7, 1912).

The writer used applications of **hot air** in 35 cases of eczema in infants, with good results. Most of the cases had already been treated with ointments and zinc oxide pastes without success. Treatment was applied for five to ten minutes, once daily, and in the intervals the affected region was covered with olive oil. Strict dietetic measures should be enforced during treatment. Perlmann (*Munch. med. Woch.*, Jan. 9, 1912).

The writer found that it is unsafe to apply the **X-rays** without a filter in

the treatment of eczema. Kuznitsky (Berl. klin. Woch., Feb. 14, 1916).

The writer has given 1 to 8 **X-ray** exposures in 28 cases of chronic eczema which had proved refractory for from 1 to 15 years to other measures. He gave a  $1\frac{1}{4}$  H unit exposure; 50 per cent. seem cured. Penso (Nederl. Tijdsch. v. Geneesk., Dec. 29, 1917).

The **X-ray** at the Finsen Light Institute at Copenhagen failed to display any actual curative action but it had a very welcome symptomatic effect. It banished the pruritus, and the peace thus obtained gave the eczema a chance to heal under local measures. The effect was only symptomatic and did not last more than 6 or 7 weeks in their 168 cases. Permanent recovery was observed in only 58; there was recurrence or renewed flaring up of the eczema in all the others. S. Lomholt (Hospitallstidende, Nov. 5, 1925).

For oozing surfaces, two to three applications of solutions (3 to 10 per cent.) of **silver nitrate** are often helpful.

In infants the face and scalp are by far the most common sites. The disease may, however, occur upon any part at any age. The treatment in regional eczema is essentially the same as the treatment of eczema of any part, common sense suggesting selection or avoidance which the character of the region may indicate for instance, upon hairy parts, as the scalp. Ointments containing large percentages of pulverulent substances, should not be employed. **Thyroid gland** is useful in sluggish cases, particularly where the stigmata of hypothyroidism are present.

The eczema in infants and young children may be due to strong soap, mustard, woolen garments, exposure to moist and cold air, excessive perspiration, parasitic disease, discharges from the navel, ears, or nose. Children may tolerate 8, 10, or 12 ounces

of milk daily, but when a larger amount is given, eczema results. A gradual increase may establish tolerance. Some infants possess no tolerance whatever for orange juice, which may cause red scaly patches about the mouth and erythema of the cheeks and other parts of the body. Beef juice acts in like manner. Butter fat, milk and cane sugar, and orange juice have been proven by elimination to be the most frequent dietetic cause of eczema. Cow's milk protein is a rare cause. The most stubborn eczema due entirely to external agencies is the *eczema intertrigo*. Such infants should be taught to **evacuate the bowels night and morning**. Over the genitals absorbent cotton is placed to collect the urine, and **citrate of potassium** given internally. **Unguentum aquæ rosæ** containing white wax, 10 per cent., is effective. The involved areas must be protected from scratching and irritation. In breast-fed infants, the first step should be to examine the mother's milk, and, if a high fat content is found, to reduce it through dieting processes. Such children are rarely cured unless they are weaned. Yet it is not advisable to wean a thriving baby because of eczema. In the bottle fed, the best results are obtained by the use of **skimmed milk** cooked with starch, preferably rice or wheat. A high protein and a high starch food may be given, often with addition of olive oil to raise the caloric content. As early as the seventh month, squash, carrots, and mashed potato can be added. The salt of fresh vegetables possesses therapeutic value. In children past the bottle age, treatment is along the same lines. Among the drugs, **potassium citrate**, sufficient to neutralize the urine, is the best. C. G. Kerley (Med. Rec., June 17, 1916).

Sajous states that a perfect secretion of the thyroid is necessary for 1, proper relationship of the amount of fat to the rest of the body; 2, proper nitrogenous metabolism of the body; 3, proper health and functions of the skin and its appendages, hair, nails,

etc. Hence, deficient secretion is apt to produce disturbances of skin functions and to interfere with the metabolism of proteins and fats. In a personal case in a child which had resisted all treatment, a complete cure was obtained with **thyroid**. Fairly large doses should be administered at first, in order to remove results which have been produced by deprivation of thyroid secretion. Later, smaller doses are given to maintain a normal equilibrium and prevent a recurrence. Following improvement, the dose of thyroid which at first was sufficient later becomes an overdose, the patient consuming his own fat. Edelman (N. Y. Med. Jour., Mar. 9, 1918).

The writer recommends small repeated doses of **X-rays to the thyroid gland** in cases of chronic eczema. He found it useful especially in the cases not responding to the ordinary local treatment. C. Guarini (Giorn. ital. d. mal. ven. e delle pelle, p. 1152, 1923).

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AND

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**EDEMA.** See ASCITES AND EDEMA.

**EDEMA, ANGIONEUROTIC.**  
See ASCITES AND EDEMA.

**ELATERIUM AND ELATERIN.**—Elaterium is a sediment deposited from the juice of the squirting cucumber (*Ecballium elaterium*, Richard). This sediment, when dried, appears in friable cakes about  $\frac{1}{10}$  of an inch in thickness, flat or slightly curled, and of a pale-green, grayish-green, or grayish-yellow color, the yellow tinge appearing when the drug is old. Its odor is feeble and its taste bitter and slightly acid. It is slightly soluble in alcohol, ether, chloroform or benzene, but insoluble in water. *Elaterin* (elaterinum—U. S. P., B. P.) is the active principle of elaterium, being found therein in amounts varying from 5 to 40 per cent. It is a neutral principle and appears as minute, white scales or prismatic crystals, without odor, but of a very bitter and acrid taste. It is freely soluble in chloroform, slightly soluble in ether and

alcohol, and insoluble in water. Elaterin is preferred for administration because of the great variability in strength of different specimens of elaterium.

#### PREPARATIONS AND DOSE.—

*Elaterinum*, U. S. P. (elaterin). Dose,  $\frac{1}{20}$  grain (0.003 Gm.)

Formerly official was:—

*Trituratio elaterini*, U. S. P. IX (trituration of elaterin), composed of 1 part of elaterin to 9 parts of lactose. Dose,  $\frac{1}{2}$  grain (0.03 Gm.).

**PHYSIOLOGICAL ACTION.**—Elaterium is a decided irritant to the mucous membranes and also to the skin, and frequently causes ulceration of the fingers and eyes in those working with it. When given internally its chief action, in man, is to produce profuse, watery stools. It is said that this drug also produces a purgative effect when applied externally. Small doses act as a stimulant to the mucous membrane of the stomach and intestine, increasing their secretions. It is also said to act as a stimulant to the liver and pancreas. When given in proper doses, these large, watery evacuations occur without undue pain or any apparent gastrointestinal irritation, and for these reasons elaterium claims first rank as an hydragogue purge.

**POISONING BY ELATERIUM.**—In large doses or in debilitated persons its use may produce so much prostration and exhaustion as to demand the exhibition of stimulants and other supporting measures. In addition to nausea, vomiting, excessive purging, and exhaustion, the use of too large doses of this drug may even be followed by death from gastroenteritis. Debility from old age or other causes and gastrointestinal irritation or inflammation contraindicate its use.

The subcutaneous use of elaterium, although capable of producing catharsis, is not advised, on account of the severe local irritation and inflammation thereby induced.

**TREATMENT OF ELATERIUM POISONING.**—The treatment of poisoning by this drug is practically that of gastroenteritis. **Morphine** should be given hypodermically, and **hot applications** made **over the abdomen** to allay pain and control the irritation and diarrhea. Especial care should be had in the selection of a proper **diet**. Bland, easily digested, and unirritating articles of food should be selected.

**THERAPEUTICS.**—Elaterium has been used in conditions demanding depletion, but salines are usually preferable in such cases; the use should not be continued if the stomach becomes disordered or the appetite impaired. It should never be used in cases of debility or marked exhaustion, and may be followed with advantage by alcoholic stimulants soon after its action is manifest. Its use is suggested in **cerebral congestion** on account of its depletant and derivative action. In **poisoning by narcotics** and in **acute alcoholism** elaterium is indicated when the emunctories are not acting freely.

It should not be used in cases of ordinary constipation, on account of its violent action. It is also contraindicated in inflammation of the stomach and intestines, in extreme exhaustion, any weak heart condition, and during pregnancy.

In **ascites** and **dropsical effusions** elaterium is of great value, though one the use of which demands much care and judgment. In dropsy depending on **aortic, obstructive, or regurgitant disease** it is especially useful, given in small doses at first, beginning with gr.  $\frac{1}{20}$  (0.003 Gm.) and increasing the dose on alternate mornings at say 5 o'clock, so that its action is finished by noon. This is claimed, by Hyde Salter, to quiet the heart, relieve the dyspnea, lessen the pulmonary congestion, and diminish the hydrothorax.

**Uremic poisoning** is much benefited through the use of elaterium, as it aids the elimination of the uremic poison by the bowel. It is especially indicated when uremia is associated with dropsical effusion.

In **pulmonary edema, pleurisy, and pericarditis**, the hydragogue catharsis induced by elaterium sometimes proves beneficial.

S.

**ELECTRIC CHOREA.** See CHOREA.

**ELECTROTHERAPEUTICS.**—While electricity has long been used in the treatment of disease, and inventions in appliances for electrotherapeutics are in some measure commensurate with those used for industrial purposes, the use of electricity in medicine is still largely discredited or ig-

nored by a considerable portion of the medical profession. Several factors have contributed to the production of this condition of affairs, prominent among which has been the disappointment caused by its failure to produce impossible results which were previously expected of it. The reaction from this disappointment was accentuated by the fact that irregular practitioners have continued to exploit it and claim for it obviously unreasonable powers. Many medical colleges have only the most perfunctory courses in electrotherapeutics, or some none at all, and medical graduates frequently start in practice with little knowledge of the physics of electricity, and less of its physiological effects when applied to the living body in the various modalities. So it has come to pass that electricity is considered by many to be useful in any large degree only to the "quack," or to have its chief value in the psychic effect produced by its use. It is much to be regretted that so much emphasis has been placed on the so-called "psychic" effects of the various applications of electricity. Not only is the scientific knowledge of the physiological and therapeutic effects of the different modalities sufficiently established to justify their rational application for specific results, but the modern status of psychotherapy does not justify the blind and indiscriminate use of a force which is mysterious, not only to the patient, but too frequently to the physician applying it.

Electricity has undoubtedly a very distinct and rather wide field of usefulness as a therapeutic agent, but one which can be successfully utilized only when its properties, physical as



well as physiological, are well understood. Although the limits of this chapter prohibit a detailed presentation of the subject of electrophysics, certain fundamental considerations of this phase of the subject are required.

### GENERAL CONSIDERATIONS.

*—Nature of Electricity.*—As is the case with all of nature's forces, an ultimate knowledge of electrical force is lacking; it is only known by its manifestations, and from these certain rules or laws have been formulated. By means of these laws are explained the relationship between the different forms or currents of electricity, and the fact that all of these different forms are essentially the same force manifesting itself in different ways according to the source by which it is generated or the influences to which it is subjected. And by practical utilization of these laws it is possible not only to regulate and measure the currents applied, but also to have available from a single source several currents having different properties.

*Electric Potential.*—The character of an electric current is determined largely by its potential, that is, its ability to overcome resistance. There are many analogies between hydrostatics and electrodynamics, and just as the force with which water flows from an opening in a pipe depends on the pressure of water within the pipe, so the potential of an electric current depends upon the pressure or "voltage" of its source of supply. As with water, the smaller the opening in the pipe the less is the actual amount that escapes with a given pressure, so with electricity the greater the obstacle to its passage the smaller the amount of the current

which passes through a conductor with a given voltage.

### *Resistance and Intensity of Current.*

—Although electricity is capable of traversing in some degree all kinds of matter, some materials, such as glass, amber, rubber, etc., offer enormous resistance to the current, and are called non-conductors, or insulators; other materials, as metals, and especially copper, offer very little resistance, and are called conductors. But all conductors offer a definite amount of resistance which varies directly with the length of the conductor and inversely with the area of its cross-section. As will be readily seen, the amount of the current passing through a conductor will depend on two factors, viz., the potential and the resistance, varying directly with the former and inversely with the latter. The units in general use for measuring the potential, the resistance and the amount of the current are, respectively, the volt, the ohm, and the ampère. One ampère represents a definite amount of force passing through a circuit; it is a unit of intensity. An ohm represents the resistance offered to an electric current equivalent to that of a column of mercury with a cross-section of 1 sq. mm. and 106 cm. long; and a volt represents the potential necessary to force 1 ampère of current through the resistance of 1 ohm. From this is formulated Ohm's law, which is

$$E$$

$C = \frac{E}{R}$ , or, transposed,  $E = CR$ , and

$$R$$

$$E$$

$R = \frac{E}{C}$ , in which  $C$  = current in am-

$$C$$

pères,  $E$  = potential in volts, and  $R$  = resistance in ohms. A thorough

comprehension of the application of Ohm's law is essential to a working knowledge of electrotherapeutics as well as any other branch of electrical science.

*Polarity.*—Electricity, whether in motion or at rest, manifests two opposing states—a positive and a negative—which tend to mutually neutralize each other. If an electric current could be said to have any direction of flow, it may be conceived as passing from the positive to the negative states or points in a circuit. As will be considered later, in certain currents the effect of this polarity is lost by reason of its rapid alternations in a given circuit.

*The constant or direct current* is a current in which the flow of electricity through the conductors is smooth and continuous, the polarity remaining fixed. Medically it is used only in small amounts, the 110-volt D. C. commercial current (generated by dynamo) being adequate for nearly all purposes in which the constant current is useful. A battery of from 40 to 60 cells, or a storage battery, may be used to furnish this form of electric force, which is also called "galvanic" or "voltaic" electricity. In the application of the direct current the intensity is regulated by a rheostat, by means of which a varying amount of resistance is interposed in the circuit and the ampèreage correspondingly reduced. As the intensity of current required for medical purposes is so small, the unit of measure employed is the milliampère, which is  $\frac{1}{1000}$  of 1 ampère, and the milliamperemeter is the instrument which records the amount being used.

*The alternating current*, so largely used for commercial purposes, is gen-

erated by dynamos, and is characterized by a rapid succession of alternations in the polarity or direction of flow of the current, usually 60 cycles (120 alternations) per second. This current is unsuitable for many uses to which the direct current is applicable, but has special uses of its own, and is readily transformed to any desired potential. It is the standard commercial current where electricity is transmitted long distances.

*Induced Currents.*—By induced electric currents are meant those which are produced in circuits which have no direct or metallic connection with the source from which they are derived. If the conductor or wire of a circuit carrying a direct current is closely parallel to part of another circuit having no independent source of supply, each time the flow is interrupted or started in the first circuit momentary waves of electricity are induced in the second circuit. This impulse in the second circuit is in the opposite direction to that in the first when the current is started, but flows in the same direction as the first when the latter is interrupted. One of the simplest applications of this principle is the faradic coil. In this instrument a small coil of wire, the "primary" coil, in connection with a direct current is surrounded by, but has no metallic connection with, a larger "secondary" coil. A vibrator, or mechanical interrupter, in the primary circuit causes the make and break with any desired rapidity. This induced current in the secondary coil is the faradic current, and is accentuated if a core composed of a bundle of soft-iron wire is placed within the primary coil. The potential or voltage of the induced or

secondary current depends upon that of the primary circuit and the relative number of turns in the windings of the two coils. Thus, if the number of turns in the two coils be the same, the voltage in the induced is the same as that in the primary current. However, the induced current is an alternating one, the rapidity of the alternations corresponding to the rapidity of the make and break in the primary by the interrupter, and it should be stated that the impulse caused by the break is greater than that induced by the make in the primary, thus producing a certain amount of noticeable polarity in the secondary circuit. If the number of turns in the secondary is double that of the primary, the voltage is doubled, and so the voltage of the secondary circuit can be regulated at will; but with each increase in voltage there is a corresponding loss of intensity in accordance with Ohm's law. In the large Ruhmkorff coils used in X-ray work the secondary windings contain many miles of fine, carefully insulated copper wire.

The principle of induction is also utilized in transforming commercial alternating currents to any desired potential, high or low, by means of "step-up" and "step-down" transformers.

*Static Electricity.*—Static, franklinic, or frictional electricity is electric force manifested in very high potential and low intensity, but differs from induced currents of similar high voltage and small volume in having a fixed polarity, whereas the induced current is of alternating polarity. The voltage of static currents cannot be accurately measured, but is estimated by the length of the spark discharge to be hundreds of thousands of

volts for the larger machines. The ampèreage of this current, even from the most powerful machines, attains only 8 or 10 milliampères, and from the average 24 glass-plate machine 1 or 2 milliampères.

*High-frequency Currents.*—This designation applies to several currents which vary as to the potential and the ampèreage, and signifies electric currents of generally high potential of an oscillating, alternating polarity of inconceivable rapidity estimated at from 500,000 to several million oscillations per second. The principle of their formation is essentially that of a series of step-up transformers or induction coils with which are utilized condensers or Leyden jars. The rapid discharge through the spark-gap of the secondary circuit also represents the discharge of the condensers. Each discharge of these is accompanied by thousands of oscillations of alternating polarity which are transmitted to coils or "solenoids" of different types and arrangements. Of the high-frequency currents used therapeutically there are two principal types, viz., the d'Arsonval and the Tesla, or Oudin. The d'Arsonval current is of comparatively low potential and high ampèreage, the latter reaching a maximum of 2000 or 3000 milliampères. The Tesla and the Oudin currents are essentially the same, and have a potential approaching that of the static current, but differ in having an alternating character, whereas the static is of fixed polarity. It is the Tesla type of current that is utilized for the production of Hertzian waves in wireless telegraphy.

**THERAPEUTICS.**—Galvanic currents for medical use are derived

either from batteries or commercial circuits. The necessary apparatus for the control and application includes a controller in the form of a rheostat of a potential reducer, a milliamperemeter, a pole-changer, and various electrodes. These can be conveniently arranged in a portable box if a battery is used, or on a table or cabinet. The potential of the source of supply may be from 50 to 110 volts, but must be completely under control so that any desired amount of current, even 1 or 2 millampères, may be applied smoothly; otherwise, undesirable and painful shocks are produced. Since the positive and the negative poles produce different effects, it is always necessary to bear in mind the polarity of the current. By means of the pole-changer, the polarity of the electrodes may be reversed without changing their position. The electrode having a positive polarity is called the anode, the one with the negative being the cathode. The amount of current used in therapeutics varies from 1 to 200 millampères, but few operators find it advisable to use more than 50 to 60 millampères.

An important characteristic of the galvanic current is its power to stimulate muscle to contraction when applied either to the motor nerve or to the muscle itself; with small currents, contractions occur only when the circuit is made or broken, and in the normal condition are momentary and followed by immediate relaxation. The force of the contractions vary with the strength of the current, and also according to whether the anode or the cathode is applied to the muscle or nerve, or whether the circuit is made or broken. In cases of lesion, or disease of the peripheral motor

nerves, or of the motor cells from which they originate in the spinal cord (or brain-stem in the case of cranial nerves), certain changes take place in the character of the reactions which are known as the reactions of degeneration (R. D.). To test the electrical reactions of muscles, one electrode is applied to the part to be examined, the other at some indifferent point. The electrodes should be covered with cotton or felt and moistened with a weak solution of sodium bicarbonate. By the pole-changer the electrode on the part examined is made the cathode, and starting with the current at zero the rheostat is gradually regulated to slowly increase the current; at the same time alternately opening and closing the circuit by means of a breaker in the handle of the electrode. When the first contraction occurs in the muscle, note is made of the reading of the meter, and whether it occurs at the make or the break. Continuing the same way, the current is increased until contractions occur both at the make and the break, and the number of millampères is again noted. Reversing the pole-changer so that the active electrode becomes the anode, the procedure is repeated, after which the record shows the minimum current strength necessary to cause contractions with the cathode and the anode when the circuit is opened and when it is closed. The following formula expresses the normal reactions:  $\text{CaCIC} > \text{ACIC} > \text{AOC} > \text{CaOC}$ , which signifies that the cathode-closure contraction is greater (or occurs with smaller current) than the anode-closure contraction, which is greater than the anode-opening contraction, which, in turn, is greater

than the cathode-opening contraction. During the degeneration of a motor nerve and the atrophy of the muscle, beginning about ten days after an injury, both the reaction formula is changed and the character of the muscular contraction is altered. The excitability of the nerve is diminished or lost, that of the muscle is increased at first and later diminished, and the contraction itself becomes slower and extends through the muscle in a wave-like motion. The reaction formula changes, the minimum contraction occurring at the anode, as  $ACIC > CaClC > AOC > .CaOC$  or  $ACIC > CaClC > CaOC > AOC$ . With the faradic current reactions of degeneration are only manifested in a quantitative change, *i.e.*, contractions diminish in strength or disappear and gradually return with regeneration.

The reactions of degeneration are not only valuable in diagnosis, but also in prognosis, as the amount of change in the responses is an accurate indication of the degree of injury to the nerve. In a case of Bell's palsy, in which the paralysis of the facial nerves is complete, the presence of faradic response and only slight galvanic R. D. ten days after the onset indicates rapid and complete recovery; loss of faradic contractions and reversals in the galvanic formula in a similar case would indicate slow and probably incomplete recovery.

The ability of the galvanic current to produce contractions in paralyzed muscles when all other measures fail makes it an important therapeutic agent for stimulating the nutrition and circulation as well as the regeneration of the affected nerves in **peripheral neuritides, acute poliomyelitis**, and allied conditions. Applica-

tions are made in the same manner as described in testing the reactions, using current sufficient only to cause contractions and frequently opening and closing the circuit. It is seldom necessary to use more than 10 or 15 milliamperes of current for this purpose, and daily applications should employ but a few contractions for each muscle.

**Cataphoresis.**—It has been demonstrated that medicinal substances in solution on an absorbent electrode can be forced by the galvanic current into the living tissues, or even entirely through them, appearing in the opposite electrode. This has given rise to the method of administering various medicaments called cataphoresis, for the reason that most of the substances so employed are attracted by the cathode pole. It should be noted, however, that such substances, including the metals, bases and alkalis to be absorbed, must be applied at the anode, for the reason that they are electropositive, such as acids, acid radicals, and also the halogens, electronegative substances, are applied at the cathode. Cocaine applied to a body surface (anode) produces superficial anesthesia. Solutions of magnesium sulphate by cataphoresis have been employed with success in the treatment of **flat warts**, but were unsatisfactory for the fungating type. Urethral cataphoresis, using a  $\frac{1}{2}$  per cent. solution of zinc sulphate, has been reported by Bouchet (1907) to be valuable in the treatment of **acute and chronic gonorrhea**. Salicylic cataphoresis with a 10 per cent. solution of the sodium salt at the cathode relieves the pain of **myalgias, neuralgias**, and some forms of **rheumatism** when applied over the affected area.

The current strength employed in cataphoresis is usually small, being limited by the toleration of the patient. Large electrodes allow stronger currents to be used than small ones. Massey applies the term "mercuric cataphoresis" to his method of treating **neoplasms**, but it is really a combination of cataphoresis and electrolysis, since not only is mercury deposited in the tissues, but also destruction of tissue takes place by action of the electricity. This method is employed under general anesthesia. Several zinc needles amalgamated with mercury connected with the anode are thrust into the tumor and the current is very gradually increased to 100 or even 200 milliampères, according to the effect desired. The result is a destruction of the tissue about the needles, with gradual separation of the slough and healing by granulation. The technique for this operation is important, as a sudden change of potential while the heavy current is passing would be dangerous. The indifferent electrode is very large and covered with wet clay, or kaolin.

**Electrolysis.**—One of the manifestations of the galvanic current is the decomposition into their constituent elements of substances through which it passes. This is exemplified by the liberation of hydrogen and oxygen at the surface of electrodes submerged in water, H from the cathode and O from the anode. When galvanism is applied to living tissues by means of needles or small electrodes, local electrolysis occurs amounting to necrosis if the application is sufficiently strong or prolonged. The action differs at the two poles, that at the anode having the character of an acid

burn, that at the cathode of a caustic alkali. The electrolytic action of electricity is adapted to the **removal of superfluous hair** and the destruction of various small **warts, nevi, sebaceous cysts**, etc.

In this form of application small potential is required, about 10 volts usually being sufficient, and a few dry cells or a storage battery answer very well. A volt-controller should be used if the 110-volt industrial current is utilized. A rheostat and meter are also required. Gold or iridoplatinum needles are advisable, since steel ones are attacked by the chemical action of the fluids liberated. Either unipolar or bipolar applications may be employed. In the former the indifferent electrode may be held in the hand of the patient. In bipolar applications two needles attached to one handle are insulated from each other and each is attached to one of the poles of the circuit.

In **removing superfluous hair**, unipolar electrolysis is used, and, with no current flowing, the needle, connected with the negative pole, is very carefully inserted alongside the hair directly into its follicle to the bottom. The current is slowly turned on, using from 1 to 3 milliampères of current. A slight froth appears around the needle, and there is always some discomfort or pain connected with the operation. Cocaine cataphoresis may be utilized on the surface treated, for the comfort of the patient. Hairs close together should not be selected for a single treatment, as soreness or scarring is likely to result, and in any event slight soreness and redness may last for a few days and minute temporary pitting occur.

For the removal of **warts and moles**

the cathode needle is thrust through their structure near the base; the current of about 10 milliamperes is then passed until the surface is blanched. Two or more needles on one electrode are used if the wart is large. The same precautions are employed in turning the current on and off as with all other treatments by electrolysis,—the electrodes should not be applied nor removed while the current is turned on. For **nevi, port-wine stains**, etc., bipolar electrolysis is employed.

In the treatment of urethral stricture by electrolysis the object is not to destroy tissue, but only to soften the constrictions by the cathode current to the point of making them dilatable. For this purpose Newman's olivary urethral bougies with insulated stems are employed, and when in place against the stricture a current of about 5 milliamperes is turned on, at the same time making gentle pressure until the bougie passes through the constriction. The size of the bougie to be selected should have only slightly greater diameter than the caliber of the stricture. Treatments may be given at intervals of about one week.

For **esophageal strictures** of traumatic or caustic origin treatment similar to that for urethral strictures may be employed with success.

**Galvanocautery.**—Either the direct or alternating current may be utilized for the galvanocautery, which depends upon the heating to incandescence the platinum electrode by the passage through it of a current of heavy ampèreage, but small voltage. From 10 to 20 ampères are required for ordinary work, and this can be obtained from a 6-volt current if the

resistance is sufficiently low. Similar ampèreage from high-voltage currents is wasteful of energy and dangerous to use. The source of current may be either bichromate cells or storage battery wired in series parallel; or where the commercial 110 volts D. C. is utilized, a combined motor and generator which delivers current of low voltage is advisable. Suitable current for galvanocautery is readily obtained from the commercial 110 volts A. C. current by means of a step-down transformer. The galvanocautery is applicable where actual cautery is needed, electricity playing no part in the application.

**The Faradic Current.**—A faradic coil may be operated by direct currents of from 4 to 110 volts. Even a single voltaic cell will furnish sufficient current to cause powerful muscular contractions and painful sensations. The high voltage of the street current (110 volts D. C.), when regulated by resistance (rheostat), works satisfactorily, but the strong sparking at the interrupter rapidly burns out the platinum contact points. A voltage-controller may, therefore, be used with advantage to reduce the current to about 6 volts. The commercial alternating current will operate a faradic coil, but the result is unsatisfactory, as the induced current from it is very jerky and uneven. Various forms of apparatus have been suggested to convert the alternating current directly into the galvanic, but though the so-called converters may work fairly well for a time, they deteriorate, get out of order and need renewal, and are generally a nuisance. Where only the alternating current is available, the only practicable way of obtaining dependable galvanic elec-

tricity for the faradic coil, as well as for other uses, is by means of the motor-generator, a combination of motor operated by the alternating current connected with a dynamo which generates the direct current.

The chief effect of the faradic current is its power to cause muscular contraction. With a vibrating interrupter the electric impulses are so rapid as to produce a tetanic contraction of the muscles to which it is applied; when the interruptions are slow, individual momentary contractions are produced. When a motor nerve is degenerated, the muscles it supplies lose their irritability to the faradic current, as was mentioned in discussing the reactions of degeneration.

By virtue of its property of causing muscular contractions, the faradic current is widely applicable in stimulating **weak, paretic or paralyzed muscles**, and by general application and by means of baths for its tonic effect.

On the sensory system, rapidly interrupted mild currents cause a rather pleasant, soothing sensation of vibration, but stronger currents, especially when applied with a wire brush or a pointed metal electrode, give rise to severe pain. Thus, by its sensory effect, the faradic current may be utilized either as a sedative or as a stimulant or counterirritant. Applied at the site on **neuralgias** with a strength moderately painful for from five to ten minutes, much relief is often obtained.

**Static Currents.**—The true static current can only be obtained in sufficient amounts for therapeutic use from the static or influence machine, which consists of a series of insulated

glass, mica, or fiber plates revolving rapidly in close proximity to other similar plates. The electricity is delivered at the terminals in the form of currents of exceedingly high voltage, but low ampère and fixed polarity, and which will pass in sparks between the poles through many inches of air space. The static machine is operated by an electric or water motor, and should be inclosed in an air-tight case to exclude moisture, which will prevent its working. In prolonged wet weather, or in damp locations, the static machine may refuse to charge in spite of all precautions. It is well to keep within the case several dishes containing about 10 pounds of well-dried calcium chloride, which should be dried again as often as it becomes soggy with moisture. Much heat is required to dry this substance on account of its attraction for water. For quick starting in emergencies, a 4-quart pail filled with equal parts of chopped ice and salt hung from a hook in the top of the case, or placed on a dinner plate on the bottom, can usually be depended upon. Large quantities of water condense and freeze on the surface of the pail, which must be removed before the frost melts. The case should be opened and closed quickly. A hygrometer within the case is of value in indicating the humidity and the efficiency of measures used to reduce it.

The output of a machine in good working order is determined by the number and size of the revolving plates and the speed at which they are run. There are several different forms in which static electricity may be applied therapeutically, depending upon the manner in which the patient



is connected with the apparatus, and are divided into three types, the disruptive (sparks), the convective, and the conductive.

*Disruptive discharges*, or static sparks, are administered by placing the patient upon an insulated stand to which the positive pole of the machine is connected. With the opposite pole grounded, the sliding rods of the spark-gap are separated beyond the sparking distance, and the patient's body is approached with the ball electrode with a chain attached reaching to the floor. The electricity passes in sparks between the patient and the electrode, and their size can be regulated by the speed of the machine, or by the more or less complete grounding of the electrode and of the negative pole of the machine. The strongest possible sparks are obtained by connecting the electrode by chain with one pole of the machine and the insulated table with the other. This method of application is more or less disagreeable, and sparks should not be drawn from sensitive areas nor from bony prominences on account of the pain produced. The effect of the static spark is to cause a momentary muscular contraction, a sharp or sometimes pounding sensation, and a small point of irritation on the skin for each spark contact. Repeated sparking at one small area will produce vesication. Static sparks are applicable principally in localized **muscle spasms** and **myalgias**, to cause contractions of **atonic muscles**, and to produce reflex effects.

The *convective discharges* include the "static bath," "static insulation," and the various "breeze," "spray," and "brush" discharges. The arrangement of the patient is the same

as for the sparks except that either no electrode at all is used or only such as cause no spark, as pointed metal or those of material having great resistance, such as wood, etc. Static insulation, or static bath, may be either interrupted or constant; in the former case the spark-gap is reduced until sparks pass causing the patient's body to be alternately charged and discharged with varying rapidity. When continuous, the spark-gap is widened and the patient is constantly charged with electricity which escapes into the air. The breeze, spray, and brush discharges are modifications of static insulation, grounded electrodes of pointed metal (for breeze and spray) or wood being held near to the patient, causing a rapid escape of electricity, which gives the sensation of blowing air, warm or cool, or of hot sand in the part which the electrode approaches.

Static insulation gives the patient a mild, pleasant sensation, often relieving headache and producing drowsiness. The spray and brush discharges are mildly stimulating to the skin, relieve **pain**, and promote the healing of **sluggish wounds** and **ulcers**.

The *conductive discharges* include the *static induced currents* and the so-called "wave currents." For the production of the static induced current, each pole of the machine is connected with the inner armature of a Leyden jar, the outer armatures being the source of the induced current. With each discharge at the spark-gap the inner coatings of the Leyden jars are charged and discharged, producing oscillations of a to-and-fro character in the outer coatings. Electrodes connected with these give a current having much the character of

the faradic current, *i.e.*, rapidly alternating and of high potential, and its strength depends upon the size of the jars, the speed of the machine, and the length of the spark-gap; there is, therefore, a very wide range of adjustment. The patient is not insulated in applying this current. The therapeutic application is practically the same as that of faradism.

The *wave currents*, typified by the Morton wave, were so named because in its application Hertzian waves emanated from the patient. The connections for this current are made, after closing the spark-gap by moving the sliding rods, by placing the patient on the insulated platform, grounding the negative pole of the machine, and applying the positive electrode directly to some cutaneous surface. On separating the sliding rods, the patient's body will be charged with positive electricity, which escapes with each discharge of the machine through the spark-gap; it is by regulating the length of the sparks that the effects are controlled—the longer the sparks, the more powerful the effect. For the more vigorous treatments the skin contact should be large, using metal plates of molding tin, or lead-foil, to the body surface to be treated; strong currents through small skin contacts cause disagreeable muscular contractions, and separation of the electrode from the skin surface causes very painful sparks.

The effects of the wave currents are local and general. The local effect is manifested mainly in muscular contraction, varying in degree and extent according to the length of spark and the area of electrode and skin contact. The frequency of contraction varies

with the rapidity of the spark discharge. The general effects consist of a sensation of vibration throughout the body, and are said to counteract **deficient metabolism** and reduce **high blood-pressure**. The wave current is a very desirable means of causing muscular contractions, as the effects are powerful and penetrating and practically painless if the electrode is sufficiently large. Hence its reputed value in **muscular atony**.

*Static high-frequency currents* are derived from accessory apparatus, as the solenoid or resonator, connected with the poles of the static machine, and will be considered later.

**High-frequency Currents.**—As has already been stated, high-frequency currents are essentially characterized by high potential and inconceivably rapid oscillations of alternating polarity, which is made possible by the discharges from condensers or Leyden jars. Almost any source of electric supply may be utilized for the production of high-frequency currents, but with varying degrees of efficiency. When the direct or galvanic current is used, a Ruhmkorff or X-ray coil may be employed. With this apparatus the primary circuit is interrupted by a mechanical or electrolytic interrupter, and the terminals of the secondary circuit connected with two condensers. The opposite sides of the condensers are connected with the extremities of a coil called the d'Arsonval solenoid, with which is also associated another (the Tesla) coil, or the Oudin resonator. When the alternating current is used, it may be converted into the direct current by means of a motor-generator and utilized as above, or may be directly transformed into a high-po-

tential current by means of a step-up transformer, the secondary terminals of which are connected with condensers and solenoid. In this arrangement the alternations of the primary current serve as interruptions and the mechanical or electrolytic interrupter is not employed. In each of the above arrangements an adjustable spark-gap in the secondary circuit discharges the condensers and regulates the voltage and frequency. With the static current the poles of the static machine are connected with the condensers, and these with the solenoid, as previously described.

The currents of high frequency are of oscillating, alternating character, and vary in potential and ampèreage according to the source of original supply, and also according to the terminals employed. The static high-frequency currents have the smallest ampèreage, registering only a few milliampères, while the transformer apparatus furnish d'Arsonval currents of 2000 to 3000 or more milliampères.

For rendering available the different modalities, or types of current, terminals are placed on the apparatus connected with the various coils. Thus, the two terminals of the secondary winding furnish a modified faradic current having high potential, the thermofaradic. Connections with the extremities of the d'Arsonval solenoid furnish the d'Arsonval current, which is of comparatively low potential and high ampèreage. Usually only one terminal of the Tesla coil or Oudin resonator is employed, and the current from this is of very high potential, but low in ampèreage.

#### *Effects of High-frequency Currents.*

—It is to be noted that there are

marked differences characterizing the action of high-frequency currents as compared with other electric modalities. In the first place the electrolytic action, so prominent in the galvanic current, is entirely lacking in the high-frequency, its energy being expended in generating heat rather than chemical effects. A high-frequency current that will not discolor a solution of potassium iodide and starch through which it passes may be capable of roasting a potato, cooking an egg or a piece of meat. A galvanic current which would produce only an insignificant amount of heat, if passed through the same solution, would decompose the iodide and discolor the starch. Again, the galvanic currents in which the potential is suddenly changed, and alternating currents of all kinds except the high frequencies, have for a prominent characteristic the ability to cause muscular contraction. The high-frequency currents, on the other hand, probably because the vibrations are above the nerve register, produce no muscular contractions even with the strongest currents.

There are several methods of applying the high-frequency currents for therapeutic purposes, according to the particular action desired. In general, the results obtained may be divided into those due to constitutional effect and those where the effect is local. For constitutional effects autocondensation and autoconduction are the principal methods used.

*Autocondensation.*—In this method the d'Arsonval current is used, and the patient is placed upon a special chair or couch, the cushions or supporting surfaces of which have a

**lining of metal**, over which is placed a heavy, insulating layer. One of the terminals supplying the d'Arsonval current is connected with the metal lining of the chair or couch, and the other with the body of the patient, usually the hands. A meter is connected in series with the patient, and with the more powerful currents will register 1000 or 2000 milliamperes. The patient feels little or no sensation, although vacuum tubes placed near him will be strongly illuminated.

For *autoconduction* no contact of any kind is made with the patient, but he sits within the spirals of a large coil of wire, the terminals of which are connected with those supplying the d'Arsonval current; the effect is similar to that of autocondensation. These two forms of treatment are most largely applied to reduce **high blood-pressure** and for **deficient metabolism**. After applications of from ten to thirty minutes there is a distinct rise in temperature, excretions are stimulated, and the blood-pressure notably reduced in cases of hypertension. The static currents are unsuitable for this form of application, as the ampère is insufficient for any decided effect.

*Diathermy*, or *thermopenetration*, signifies the thermic effect of the d'Arsonval current, which is very considerable under certain conditions. This also requires heavy ampère, for which the static current is inadequate. Two metal electrodes are applied to the part of the body that requires treatment, and the current is increased until the desired result is obtained. There is little danger of doing harm, as the toleration of the patient is reached before any burn is produced. The effect appears to be

purely thermic, and is applicable to conditions where heat is indicated. By this method the penetrating effects of heat can be produced more effectively than by any other method.

High-frequency currents may be applied locally by means of various electrodes, of which the glass vacuum tubes have the widest range of use. By means of these either the d'Arsonval or the Oudin current may be applied, giving both constitutional and local effect. The constitutional effect is similar but less than that produced by autocondensation, and the local effect varies with the type and strength of current used, and with the manner of application. With the electrode in contact with the skin the only sensation caused is that of warmth, the d'Arsonval current being the more penetrating. If the vacuum electrode is held at a distance from the surface, a multitude of fine sparks are discharged into the skin, producing a sharp sensation and a marked hyperemia of the cutaneous surface.

From metal electrodes the sparks are sharper and have a cauterizing effect. Electrodes connected with the Oudin current held at some distance from the surface cease to discharge sparks, which are replaced by a spray-like discharge called the *effluve*. The sensation produced is very mild and the effect superficial and mildly anesthetic.

Applications of the high-frequency currents, both the d'Arsonval and the Oudin, are of great value in the treatment of painful conditions, such as **neuralgia**, **neuritis**, **myalgia**, and **arthritis**; and also for many cutaneous affections, as **eczema**, **ulcerations**, **lupus**, etc.

**Fulguration.**—The cauterizing effect of the high-frequency spark from pointed metal electrodes has been utilized for the destruction of small **neoplasms**, **angiomas**, etc., and has considerable latitude of application. With the d'Arsonval current bipolar application may be made, placing a large neutral electrode opposite the area to be treated. Unipolar applications are less penetrating. The pointed electrode is held at or near the surface to be treated, the vitality of which may be rapidly destroyed. If the bipolar method is used deep cauterizing effect can be produced with almost the same accuracy as with a knife. The destroyed tissue ultimately sloughs and the wound heals by granulation. The effect is not selective, but destroys healthy as well as abnormal tissue. With the Oudin current long, heavy sparks may be used by bipolar application, giving a more superficial cauterizing effect.

The term *desiccation* has been given by Clark to his method of employing the high-frequency current from high-powered static machines for the destruction of tissue. With a carefully adjusted current from the resonator, by means of short, rapid sparks from a pointed electrode, the effect is sufficient heat to devitalize but not to burn the tissues.

**Sinusoidal Currents.**—In some alternating currents the transitions from one phase or polarity to another is sharp or abrupt, rendering the effect biting and unpleasant when applied therapeutically. An alternating current in which the changes in polarity are gradual has been termed the sinusoidal current because the graphic curve of the wave is similar to the

geometric sine curve. In therapeutics sinusoidal currents are employed having a potential with a maximum of about 110 volts, and are usually generated by special generators. The commercial alternating current can be utilized by means of transformers and controllers, but is not entirely suitable for this purpose. The value of this current in therapeutics depends upon its faculty of producing a maximum of muscular contraction with a minimum of discomfort to the patient, in this respect resembling the static-wave current. The sinusoidal will often cause contractions in muscles where faradism fails on account of a partial reaction of degeneration associated with disease of the motor nerves. It may be found useful, therefore, in **muscular paresis** or **paralysis**.

**Magnetic Wave Currents.**—The magnetic field of electromagnets, actuated by an alternating current, has been utilized therapeutically, placing the patient between two magnets of opposite polarity. Although no sensation is felt by the patient, this treatment is said to have a general effect of **deficient metabolism** and reducing **high blood-pressure**.

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**ELEPHANTIASIS.**—Elephantiasis arabum; pachyderma; elephant leg; Barbadoes leg.

**DEFINITION.**—Elephantiasis is a chronic hypertrophic disease of the skin and underlying tissue due to obstruction of the lymphatic channels by parasites or other causes, and resulting in enormous enlargement and thickening of the part, with or without papillary overgrowth.

**SYMPTOMS.**—The term “elephantiasis” was used by the Greeks to designate the malady now called leprosy. Elephantiasis græcorum is, therefore, to be distinguished from elephantiasis arabum. The most frequent seats of elephantiasis are the lower extremities, although the penis, scrotum, labia, and clitoris may be affected, and more rarely the arms, lips, tongue, or ears.

heat, and pain. The condition may represent a dermatocellulitis, a lymphangitis, or a phlebitis. After some days the inflammatory phenomena subside, but the affected part is observed to be larger than before. Similar attacks may recur from time to time, at intervals of weeks or months, the affected part increasing in size after each attack. Finally, a state of chronic hypertrophy is



Elephantiasis. (W. K. Hunter.)  
(Glasgow Medical Journal.)

There are two forms of the disease, the one, *endemic*, is parasitic in origin and indigenous to the tropics; the other, *sporadic*, is due to inflammatory obstruction of the lymphatic or blood-vessels and observed in various countries. There is also a congenital form of elephantiasis, which is extremely uncommon. The tropical form is rare in the United States; we will, therefore, restrict our description to the ordinary variety.

The disease usually begins as an erysipelatoid inflammation, accompanied by fever, redness, swelling,

reached, the skin and subcutaneous tissue are enormously thickened, and the member greatly increased in diameter.

The skin is glossy and tense and the deeper structures resistant and dense, as a result of which digital pressure produces but slight indentation or none at all. The surface may be pigmented, exhibit warty excrescences or thickly studded papillomatous vegetations. These consist often of lymphatic varicosities, the elevations occasionally discharging a chylous or milky fluid. Between the

papillary overgrowths, fissures of varying depths are observed.

Maceration of the epidermis and the collection of decomposing sweat, sebum, and effete products give rise to an offensive odor, particularly where habits of cleanliness are not observed. There is, as a rule, no pain, although during the acute inflammatory exacerbations it may be severe. The enormous weight of the hypertrophied part may make locomotion difficult or even impossible. The course of the affection is chronic.

**ETIOLOGY.**—The disease is most common in tropical countries, particularly Africa, India, China, Japan, West Indies, etc., where it occurs chiefly in those subject to bad hygiene and poor food. Damp, malarial districts are said to produce the largest number of cases. This is explicable upon the theory now proposed, that the mosquito is the intermediate host of the filariæ. The tropical form is due to inflammation and obstruction of the lymphatic vessels because of the *Filaria bancrofti*. The parasites are most likely to be found in the blood at night; blood examined in the morning usually fails to show the presence of the filariæ. They appear as transparent, serpentine, wriggling, worm-like creatures in a sac or sheath.

Sporadic cases may be due to inflammatory obstruction of lymphatic and perhaps other vessels, following repeated attacks of erysipelas, and as a result of cellulitis, infection from ulcers, syphilis, pressure of scars or tumors, etc. The spirochete of syphilis and tubercle bacilli are effective causal organisms of elephantiasis of the genitals due to lymphatic stasis.

**PATHOLOGY.**—There is a hyperplasia, participated in by the subcu-

taneous tissue and all of the layers of the skin. The chief change is in the subcutaneous tissue, which is enormously hypertrophied and traversed by irregular bundles of connective tissue. Where the surface of the skin is warty, the papillæ are greatly elongated. Both blood-vessels and lymphatics are enormously distended, the latter leading to dilated lymph-spaces. The neighboring lymphatic glands are enlarged. In advanced cases the muscles undergo fatty degeneration and the bones enlarge.

There are 3 distinct phases of elephantiasis: 1. The filarial infection and filarial damage to the host. 2. The defense reaction of the host. 3. The post-defense hyperplasia of lymphatics and fibrous tissue. In the phase of infectivity the young worm matures in the lymphatics. The sheathed embryos of *Filaria bancrofti* appear in the superficial blood-vessels at night and gather in the deeper structures in the day. This phase may continue for years. Albumin and casts appear in the urine. Nocturia and signs of early arteriosclerosis appear. Examination of the blood reveals a lymphocytosis.

During the second stage the gland enlarges at the site of lodgment of the adult parasites. The patient suffers from chills and a fever usually ranging from 101 to 103° F. The lymphocytosis gives way to a polymorphonuclear leucocytosis of from 16,000 to 20,000. At the end of this defense reaction the adult parasite dies and the embryo leaves the blood stream. The parasite plays no part in the elephantiasis or any other pathological process which may follow.

In the third stage, elephantiasis follows a simple mechanical blocking of the lymph spaces. It is brought about by the deposit in the intracellular spaces of chemical substances contained in the lymph. A benign hyperplasia develops, with the formation of ulcers and fissures. H. M. Stenhouse (U. S. Naval Med. Bull., Feb., 1925).

**DIAGNOSIS.**—The history of recurrent erysipelatous inflammation, with slowly progressing hypertrophy, is commonly noted in the sporadic form of elephantiasis. In advanced cases, particularly of the tropical variety, the appearances are unmistakable, the enormous enlargement of the affected member being absolutely characteristic.

**PROGNOSIS.**—In the beginning the process may at times be arrested. When the growth is far advanced, treatment accomplishes but little, though some surgical measures (see **TREATMENT**) may afford hope. Very severe cases may terminate fatally.

**TREATMENT.**—The erysipelatous attacks are to be treated by **rest, hot or cold applications, elevation of the affected member**, and the internal administration of **salines and quinine**. Quinine is especially useful in elephantiasis contracted in malarial regions. Dubriel de Broglie has recommended the internal use of 30 drops of the **tincture of ferric chloride** three times daily.

A marked reduction in size and considerable improvement in locomotion followed the use of **thyroid gland** in large doses, 35 to 40 grains (2.3 to 3.3 Gm.), subsequently reduced to 20 grains (1.3 Gm.) per day. This caused a loss in weight of 89 pounds from 410 pounds. G. G. Davis (Penna. Med. Jour., Aug., 1915).

In spirochete cases bathing with a **mild solution of mercury bichloride or sodium bicarbonate** proved useful in relieving tension, and pads of bichloride gauze in the irritation of friction. For good results, **curetting** must be done until the normal substratum is reached. Dressed with **iodoform gauze** or 1:2000 bichloride gauze, the ulcers then soon heal. Ravogli (Lancet-Clinic, June 17, 1916).

In a case of elephantiasis of the *vulva* following supposed attacks of influenza, the writer obtained *Staphylococcus albus* by puncture of the labia majora. The patient having had repeated attacks of lymphangitis, a pyogenic origin was suspected and Delbet's **vaccine** considered indicated. No filariæ could be found in the blood. Clueyrat and Deguignand (Bull. Soc. franç. de derm. et de syph., No. 8, 1921).

**Good food and hygiene, tonics, and change of climate** are important features in endemic cases. Elastic compression by means of a well-applied **rubber bandage** is the most efficient therapeutic measure. **Green soap** and the **mercurial ointments** may be rubbed into the skin. The long-continued use of the **galvanic current** has occasionally given good results.

In advanced elephantiasis of the leg one may resort to **stretching or partial exsection of the sciatic nerve**, or digital or instrumental **compression**, or even **ligation of the femoral artery**.

Elephantiasis of the scrotum is best treated by **amputation**. Various conservative surgical measures have, in addition, been introduced.

Case in which striking improvement followed **angioplasty**. A number of stout silk threads running the whole length of the limb are introduced into the subcutaneous tissue of the swollen part. The threads are completely and permanently buried. Their capillary action enables them to replace the trunk lymphatics and to transfer the excess of fluid from the area of lymphatic edema to regions where the lymphatic circulation is normal, and where consequently the excess of fluid is absorbed and carried off into the general circulation. Handley (Lancet, Jan. 2, 1909).

Case in which the writer restored the patient to active life by a combination and modification of Lanz and Oppel's methods for diverting the course of the lymph by **anastomosis between**



the **superficial and deep lymphatics**. Diamond-shaped patches of skin, 15 or 11 cm. across, were cut out of the thigh and calf. The subcutaneous tissue and aponeurosis were cut across on the short diameter of the diamond and then cut along one side line down to the muscle. This produced two triangular flaps; each was turned over and pushed into the space below between the layers of the muscle separated for the purpose with a blunt instrument. The flaps were held with a few catgut stitches in the muscles and periosteum. The skin was drawn together and sutured along the long diameter of the diamond, thus exerting compression on the lymphatics below. Rosanow (Archiv f. klin. Chir., Bd. xcix, Nu. 3, 1912).

The writer performed **Handley's operation** (*vide supra*) in 2 cases of elephantiasis of the lower extremities. The results were excellent. Great care is necessary to bring about and maintain perfect asepsis as well as prolonged absolute rest. The best results were obtained with the patient whose leg was immobilized for two and a half months. Bilim-Kolosovsky (Roussky Vrach, April 28, 1912).

The writer tried the methods of Lanz and Handley and found them useless, because there was in all his cases a very thick fascia which prevented the lymph communication between the muscles and the subcutaneous tissue. He therefore attempted to restore this continuity by removal of large areas of fascia. This was done by making long and broad **incisions** followed by the **removal of an area of fascia** corresponding. In 6 cases the operation was attended by excellent results and increased usefulness of limbs. E. Kondoleon (Zentralbl. für Chir., July 27, 1912).

Report on 31 cases of elephantiasis and 2 of **lymphedema** treated with the **Kondoleon operation** at the Mayo Clinic. An elliptical incision is made on 1 or both sides of the extremity for the removal of wide segments of skin and still wider sections of subcutaneous tissue and aponeurosis. In the case of the leg, the incision is made on the outer side from the iliac

crest to below the external malleolus. The knife then separates the skin from the subcutaneous tissue for an inch or more, and the skin is retracted to expose a wider area of tissue than the skin which is to be sacrificed. A wide quadrilateral strip of edematous fat and aponeurosis is removed *en masse*, exposing the muscle all along the incision. The superficial and deep lymphatics are thus allowed communication and the limb thereby drained. The same operation is usually necessary also on the opposite side of the leg, either at the same time or in 10 days or 2 weeks. **Rest in bed with elevation and firm bandaging** for 2 or 3 weeks simplify the operation. **Morphine**,  $\frac{1}{4}$  grain (0.01 Gm.), is given before and after the operation. The results, on the whole, were good. In many cases the extremity could be kept within normal limits by persistent use of **bandages**. Paticnic with repeated erysipelas had no recurrences of these attacks. Sis-trunk (So. Med. Jour., Aug., 1921).

For the purpose of establishing lymphatic drainage the writer brings normal and affected skin into close contact by planting a pedunculated **normal skin flap** with its subcutaneous fatty tissues into the affected site. This method is more effective in the penis or scrotum than in the lower extremity. In elephantiasis of the lower extremity, this method, together with Kondoleon's method, and the removal of superabundant tissues, has given better results than any method now in use. H. Kimura (Japan Med. World, Aug. 15, 1925).

Almost perfect result of a Kondoleon operation done 41 years before on a woman, aged 48, whose work requires almost continuous standing. He kept her in bed for nearly 3 months, with **massage**, before the operation, to get the skin and leg ulcers into better condition. He prefers Kondoleon's technic as no foreign body is left in the tissues. M. Melletti (Policlinico, Oct. 15, 1925).

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**EMBOLISM.— DEFINITION. —**

Embolism is the obstruction of some portion of the vascular system and arrest of the circulation by a plug conveyed in the blood-current. The obstructing body, which may consist of organic or inorganic material, is termed an embolus. Thrombosis and embolism are often associated, a thrombus when dislodged from its position becoming an embolus, and the latter, by deposit of coagulum, growing into a thrombus. Embolism affects arteries and capillaries and, also, the portal vein on account of the anatomical arrangement of that vessel. The exceptional involvement by retrogression of other veins and of the lymphatics will be subsequently considered.

**SYMPTOMS.**— In general terms these relate to the resulting anemia, necrosis, sloughing, sepsis, and abolishment of function. Mild degrees of embolism occasion little or no constitutional disturbance, while the local manifestations may be so slight as to render the ordinary methods of physical examination useless or inconclusive. The symptoms are manifold, however, in the severer forms of obstruction, and vary according to the character of the embolism and of the vessel or structure involved.

Cases of fatal postoperative embolism since the opening of the Mayos' clinic, September 30, 1889. The total number of deaths in the hospital for the period under consideration, from all causes, was 864, of which the fatalities from embolism were approximately 5 per cent. The mortality from embolism, based on 63,573 operations, is 0.07 per cent., or 1 death in every 1352 operations. Twenty-six of the patients were males and 21 females, the youngest being 25 years of age and the oldest 72. Forty-one of the patients had been

from two to thirty-five years subject to some form of severe chronic debilitating disease. Nineteen of the fatalities occurred within the first week after operation, 21 more within the second week, 4 in the third week, and 1 each on the twenty-sixth, the thirtieth, and the sixty-fourth days, respectively. In 36 of the cases the embolism was pulmonary, in 10 cerebral, and in 1 coronary. In 28 of the 41 cases posted, the originating thrombus was found in the field of operation or the femoral vein.

From a study of his cases and of the literature, the writer calls attention to the following general considerations: 1. Following operations, particularly on the blood-vessels, alimentary canal, and genitourinary organs, from 1 to 2 per cent. of all cases give more or less distinct clinical evidence of emboli, above 70 per cent. of which are in the lungs. 2. About 10 per cent. of post-operative emboli which give clinical symptoms of diagnostic significance cause sudden death. 3. The source of the emboli can be definitely determined by autopsy as venous thrombosis in about 80 per cent. of the cases, as cardiac thrombosis in 10 per cent., while 10 per cent. are scattering or indeterminable. 4. The most important factors are the injury of the vascular walls, slowing and stagnation of the blood-stream, the disintegration of the corpuscles of the blood from toxic substances and bacteremia. 5. In consideration of the above-mentioned factors the following precautionary measures suggest themselves: 1, the reduction of vascular traumatism to a minimum; 2, the encouragement of very early free movement on the part of the patient; 3, the preoperative administration of drugs to increase the coagulability of the blood; and, 4, measures looking toward the reduction of bacteremia. L. B. Wilson (N. Y. Med. Jour., from *Annals of Surg.*, Dec., 1912).

One of the most common forms of embolism is produced by thrombi originating in the endocardium, in atheromatous patches of the aorta,

and in the large veins of the pelvis and lower extremities. A calcareous or vegetative fragment from a diseased valve or intima in aortic obstruction or ulcerative endocarditis is a frequent source.

Equally frequent causes of embolism are fat particles from fractures of the bones, with laceration of the marrow; from contusions of the adipose tissue, and from injury to various fat-containing organs or structures of the body. Other sources of embolism are tissue fragments, pieces of a tumor projecting into a vessel, pigment particles in disorganization of the blood by malaria, and small hyaline masses occurring in burns and certain kinds of toxemia. Emboli may consist, also, of giant cells derived from bone-marrow and the chorionic villi, parenchymatous cells from the liver, spleen, myocardium, and other structures, or tumor-cells. Lastly, embolism may result from bacteria, scolices of echinococcus or other parasites, and from foreign bodies, such as air and dust. It has been claimed that embolism occurs more frequently in females than in males, and that of all the valvular lesions giving rise to it mitral stenosis is the most common.

In the writer's statistics on post-operative embolism, interventions on the prostate gave the highest percentage (4.2 per cent. in 356 patients). Absolute prevention could not be realized. Thrombosis of the saphenous vein is not very dangerous. He consented once to a herniotomy in a woman only on condition of preventive simultaneous resection of both varicose saphenous veins. The patient consented and died 10 days after operation from pulmonary embolism—perhaps because of this attempt to prevent it. *De Quervain* (Schweiz. med. Woch., May 28, 1925).

The writer studied 21 cases of fatal pulmonary embolism occurring in 12,615 operations. Necropsies in 9 cases showed a thrombosis of the femoral vein in 4. In 1 there was a thrombosis of the common iliac vein and the inferior vena cava. In 2 cases a wound inspection only was allowed, so the condition of the femoral veins was undetermined. In the remaining 2 cases, while a complete necropsy was performed, no existing thrombosis could be demonstrated. *J. A. Victor* (*Annals of Surg.*, Aug., 1925).

The location and distribution of embolism depend chiefly upon the source. Emboli in the general venous circulation usually pass through the right heart and lodge in some branch of the pulmonary artery. Those in the portal circulation are either arrested in the liver or borne to the heart and lungs, while those originating in the left heart enter the general arterial circulation and may be widely distributed to the different organs of the body and the peripheral vessels, but are most frequently found in the spleen, kidneys, and brain. As a rule, emboli follow the blood-current and finally lodge at the bifurcation of a vessel or at a point where the size of the tube renders further progress impossible, although a soft embolus impacted against a bifurcation may split into fragments, which enter the smaller branches of the artery.

Thrombosis and embolism are most common after pelvic operations. Often pleurisy, pneumonia and pulmonary abscess following operation are probably due to emboli. Large emboli almost always cause speedy death by syncope or asphyxia; very small emboli usually run a favorable course. Any sudden increase in pulse rate during convalescence, the temperature remaining about normal, suggests the possibility of thrombosis. *Dearborn* (*Ann. of Gynec. and Ped.*, Nov., 1904).

In a study of embolism due to gunshot injury to the carotid arteries, based on 14 cases, the writer found that embolic obstruction of even minor cerebral vessels may produce more serious effects and is more readily recognized than the blocking of vessels supplying small areas of the limb.

It is recognized by a systolic arterial bruit, an arteriovenous murmur and purring thrill, a pulsating swelling in the course of the vessel, or secondary hemorrhage demanding surgical intervention. Makins (*Lancet*, Sept. 23, 1916).

To the general rule above stated there are two exceptions: paradoxical and retrograde embolism.

The term *paradoxical embolism* is applied to the entrance into the general circulation of venous emboli through a patent foramen ovale or ductus arteriosus, or a perforated ventricular septum. Emboli in the lungs may be broken into smaller fragments—as often occurs in fat embolism—and, penetrating the pulmonary capillaries, enter the general circulation.

Another variety has been termed *retrograde embolism*. In whooping-cough, emphysema, and other affections of the respiratory organs in which the intrathoracic pressure is increased, with positive instead of negative pressure in the large intrathoracic veins, emboli in the form of tumor fragments, cellular bodies, microbes, or other material may be carried in a direction opposite to that of the normal blood-current. From the inferior vena cava, for instance, the plug enters the hepatic vein and lodges in the liver, while the peripheral veins of the body may be occluded by emboli coursing backward from the right heart. In such instances there is either a reversed

current from obstruction at the right auricle or successive cardiac impulses, sending the impacting body in a backward direction. In this connection reference can be made to an apparently retrograde embolism in the lymph-vessels, which is stated to be due to occlusion and dilatation of the vessels, with incompetent valves, and a consequent backward flow. Another explanation is that tumor-cells have the power of moving in this direction, the result being, for instance, malignant disease of the lymph-glands from tumors situated on the distal side.

The writer's experiments warranted the following conclusions: Thrombosis of veins of the omentum is readily produced by mechanical, thermal, and bacterial agencies. From thrombosed omental veins emboli may frequently separate, probably owing to the periodical vasodilatation and contraction associated with the ingestion of food. Emboli from veins in the omentum may, under certain circumstances, be carried up gastric veins and become impacted in the venous plexus of the submucous coat of the stomach, and determine a gastric ulcer. Beyond this it is impossible to go at present, but these experimental results prompt certain suggestions in regard to the etiology of gastric and duodenal ulcers in the human subject which can only be decided by prolonged and extensive clinical investigation. These suggestions are: That the hematemesis sometimes met with in cases of acute appendicitis is due to an acute gastric ulcer resulting from blockage of a gastric vein by a septic embolus from a thrombosed omental vein. That on similar lines the omental vessels may form the connecting link in the association of chronic gastric or duodenal ulcer with an inflammatory process in the lower abdomen. One might even go further and suggest that the relatively greater frequency of duodenal ulcer in the male is directly associated with his greater

liability to appendicular trouble and consequent involvement of the right border of the omentum, while the relatively greater frequency of ulceration of the body of the stomach in the female is associated with her exposure to pelvic inflammatory trouble which may occur on either side and may involve any portion of the omentum. The ulcers which were produced experimentally were of the acute type, and they tended to heal up readily, for the animals used were healthy and lacked the very important factors which appear to determine the chronicity of gastric ulcers in the human subject, namely, the general irritability of the gastric mucosa and the altered secretory function of the gastric glands. The occurrence of embolism of veins in the pancreas, followed by hemorrhages into the pancreatic tissue, after the injection of artificial emboli into omental veins, suggests the possibility of portal embolism playing a part in the etiology of some cases of acute pancreatitis. D. P. D. Wilkie (*Edinburgh med. Jour.*, May, 1911).

Emboli may also occur in *special locations*. Embolism of the aorta, of the superior mesenteric artery, and of the spinal cord is uncommon, and, in many instances, does not admit of easy diagnosis. Emboli may lodge in the small intestinal arteries. More frequently, the lungs and brain are involved. The kidney is said to furnish 66 to 75 per cent. of cases, and the spleen is next in frequency. In typhoid fever 6 per cent. of the fatalities are ascribed to pulmonary infarcts.

Postoperative pulmonary embolism was observed in 57 out of a total of 6871 operations in von Eiselsberg's service at Vienna since 1901. In 23 cases the fatal embolism did not become infected; in 20 cases there were infarcts, and in 14 there were embolic-suppurative processes. There were also noted pulmonary complications in 263 cases, that is, 3.8 per cent., but

of embolic nature in only 0.8 per cent. A laparotomy has been done in 24 and herniotomy in 12 of the embolic cases. In the 23 fatal embolic cases death occurred in a few minutes from the first symptoms of the embolism in 5 cases, while in 9 several hours elapsed before the fatal termination. In 3 the symptoms of embolism were observed immediately after the operation. Ranzi (*Archiv f. klin. Chir.*, Bd. lxxxvii, Nu. 2, 1908).

The writer was able to find some primary infectious focus in every case of fatal pulmonary embolism from primary venous thrombosis. In some cases the walls of the vein are inflamed, but in others infection of the blood is responsible for the intravascular coagulation. Kretz (*Med. Klinik*, Oct. 10, 1909).

Since 1899 there occurred in St. Luke's Hospital 15 cases of sudden death following operation which have been attributed to pulmonary embolism. Such autopsies as have been performed have verified the condition. Special attention is called to three main factors: The age of the patients—young individuals are more or less exempt, and if affected may perhaps recover presumably on account of the yielding elasticity of their vessels, which may allow the blood to push its way beside a clot. The age from 40 to 60 being most afflicted, we are probably dealing with conditions of vascular changes over which the operator has little or no control. Practically all those cases of embolism follow interventions below the diaphragm and even lower. Gibson (*Med. Record*, Jan. 9, 1909).

The mortality statistics of embolism of peripheral origin show a high death rate. Lenormant collected 233 cases where it had followed surgical operations, and found that 106 (45.5 per cent.) ended fatally, but such statistics undoubtedly exaggerate the mortality, since they contain a disproportionate number of serious cases. In those of cardiac origin, embolism is often a terminal event and usually indicates the beginning of the end. According to Romberg, 36 of 43 patients with heart

disease in the Leipzig Clinic, in whom a positive diagnosis of pulmonary embolism was made, died. Three striking instances witnessed by the writer raised a question as to the frequency with which they are overlooked, because their possibility is not considered in making a differential diagnosis. Some cases must necessarily escape detection because they cause no symptoms; others because they are terminal events occurring when the patient is already in a serious condition, if not *in extremis*, and the symptoms are confounded with those of the primary disease. The most characteristic symptoms are dyspnea, cough with bloody expectoration and pain, but the suddenness of its onset alone gives the first distinctive significance. The other two are so infrequent that their absence is of little importance. The discovery of physical signs of consolidation in the lungs may be of assistance in diagnosis, though a large infarction may lead to error by suggesting a pneumonic process. It may resemble one of the following conditions: cardiac asthma, acute dilatation of the heart, angina pectoris, pneumonia and pleurisy, phthisis, bronchitis and neuralgia. Sears (Boston Med. and Surg. Jour., April 28, 1910).

A study of 25 cases of fatal pulmonary embolism that occurred in the writer's service in the last eight years showed one common factor in all, *viz.*, that organs containing infectious germs were opened in the course of the operation. These germs must have found their way into gaping veins and the latter been responsible for the development of thrombosis and subsequent embolism. J. Veit (Zentralbl. f. Gynäk., Jan. 1, 1910).

Embolic infarcts may occur at any place in the lung, irrespective of the primary site of the embolus. The part most commonly involved is the lower lobe. Reye (Zentralbl. f. allg. Pathol. u. Path. Anat., Dec. 15, 1912).

Experiments have been reported which give some ground for the belief that cerebral embolism and chorea may be related as cause and effect,

but corroborative clinical evidence is wanting.

The writer witnessed 2 cases of cerebral embolism neither of which presented the characteristic symptoms. In the first case the man drank a cup of coffee, tried to stand up, and then learned that his left arm and leg were paralyzed. He did not lose consciousness at all and the paralysis soon passed away. For two days he ate, drank, and felt well. He then became unconscious and remained so until his death eleven days later. Autopsy revealed an embolism of the artery of the Sylvian fossa on the right side, with some softening of the brain. In the second case, a boy, 15 years old, convalescent from diphtheria, suddenly began to vomit frequently, became very pale, had facial spasms, finally paresis of the left side of the face, uttered from time to time a cry like the hydrocephalic cry of children with meningitis, and grated his teeth. At times he was apathetic, at other times restless. On the morning of the day of his death there was noted a slight facial paresis on the left side, vomiting, great thirst, and no paralysis of the limbs; he ate, drank, and slept well; the pupils were alike and reacted promptly. Lumbar puncture revealed nothing pathological. That evening he died and the autopsy revealed an embolus of the right artery of the Sylvian fossa, dense, dry, and extending into the finer branches of the artery. Hippel (Med. Klinik, Jan. 22, 1911).

In 2 years the writers observed 12 cases of hemorrhages affecting electrically the striate body—most of them its anterior upper part. The internal and external capsules were intact. The hemorrhages followed embolism—usually due to endocarditis. Schwartz and Goldstein (Münch. med. Woch., Dec. 11, 1925).

As to the *results of embolism*, sudden death is apt to follow the occlusion of the coronary artery or one of the large vessels in the lungs or medulla; but a fatal termination may



Gangrene Due to Thrombus.





be delayed in partial obstruction leading to thrombosis. The effects of embolism depend, therefore, upon the amount of obstruction, the character of the occluded vessels, and the particular area involved. When the anastomosis of the vessels is free, the increase of blood-pressure and the dilatation of the relieving vessels on the proximate side of the plug compensate for the transient anemia on the distal side. Thrombosis occurs before and behind the obstruction, extends in both directions to the nearest vessels, becomes organized, and reduces the involved vessel to a solid cord. Connective-tissue proliferation takes place in the vessel. The same compensatory changes occur in capillary embolism, and in both instances the damage inflicted is trivial, consisting only of the loss of a portion of the circulation. With multiple embolism, the results may be serious.

Large emboli following abdominal section usually cause speedy death by syncope or asphyxia, but small emboli usually run a favorable course. Thrombosis may result, (1) after a prolonged or severe operation; (2) as the result of sepsis in the wound; (3) without either of the above conditions. Pulmonary embolism most frequently results from thrombi in the venous system. The latter are most frequent in the leg, as in fractures and protracted fever. Emboli resulting from thrombosis of veins after pelvic and abdominal operations come next in frequency. There is practically no treatment for the severe cases. A careful study of the blood before operation, avoidance of profuse hemorrhage during the operation, and **saline infusions** after the operation may diminish the frequency of such cases. Wilmer Krusen (*Amer. Jour. of Obstet.*, April, 1906).

Two cases, the first being one of thrombosis of the superior mesen-

teric vein following operation for tubal abortion. She was seized with all the symptoms of ileus and a portion of the jejunum was resected. The only mechanical obstacle was an infarct in the intestinal wall which had narrowed the lumen of the bowel. The symptoms were not relieved and autopsy revealed the extension of the thrombosis at the site of the resection. Hedlund (*Hygiea*, Sept. 15, 1917).

A slight edema of the inguinal region may indicate thrombosis of the external iliac vein. Mahler's sign (climbing pulse) is valuable, but not always present. Getting the patient up early or exercises done in bed can hardly prevent thrombosis. T. Wyder (*Schweiz. med. Woch.*, Jan. 23, 1926).

**Infarction** results from the occlusion of end-arteries, such as are found in the lungs, brain, spleen, kidneys, mesentery, retina, and portions of the heart. Anemia with necrosis may occur, or else a transient anemia followed by a backward flow of venous blood, causing engorgement or hemorrhagic infarction. The tissue involved, or infarct, is denser than the surrounding area, wedge-shaped, red, and pulpy, with the apex pointing to the embolus. At other times the area affected is of a grayish color, the white infarct. The shape of an infarction is irregular when several vessels are blocked. These results are not uniform, however, in the case of structures supplied by end-arteries. Exceptions are noted when the surrounding blood-supply is free, as, for instance, near the root of the lung, whereas a striking example of the red infarct is found in the periphery of that organ. In the spleen, infarction is the rule, and coagulation necrosis is apt to occur in the kidney, although the affected tissue is wedge-shaped. In the brain and retina, necrosis with softening ensues. In the liver the

blood-supply from the hepatic artery suffices for a limited secretion of bile, even with obstruction of the entire portal vein. When the superior mesenteric artery is involved, infarction is the rule, while sloughing and hemorrhage occur. The ultimate effect of embolism after anemia and necrosis is the loss of tissue by sloughing, cicatrization, and absorption.

**Septic emboli**, in addition to their mechanical effects, are the carriers of infection, and when disintegrated become the distributors of micro-organisms from their point of lodgment to the system at large. Typical examples occur in septic endocarditis or in infectious embolism of the lung. Secondary infection of bland infarcts may occur. Thus the so-called metastatic abscesses have their origin, and septicemia is apt to follow. Multiple tumor growth may be caused by cells brought from a tumor of like character located at a distance, while microbic action at the seat of occlusion may so affect the vessel wall as to produce what has been termed embolic or mycotic aneurism.

**Fat embolism**, which probably occurs to a greater or less extent in all cases of bone-crushing or contusion of adipose tissue, may have no pathological or clinical significance. In mild forms the fat particles are absorbed in the pulmonary capillaries, or pass through them in subdivisions, to be absorbed in the circulation or in the spleen, liver, kidney, or other organs. When the amount of fat is considerable and widely distributed, the most serious consequences may follow. In such cases there are dyspnea, quickened respiration and pulse, and, in a word, the usual symptoms

of respiratory obstruction, which appear usually in from thirty-six to seventy-two hours. In fatal cases death supervenes upon cyanosis, delirium, and coma, with profound asthenia. The temperature, at first subnormal, may remain so or be elevated. The presence of fat globules in the urine is noteworthy and of diagnostic importance. Fat embolism is to be differentiated from shock, acute pulmonary and renal congestion, acute septicemia, and ether anesthesia. The prognosis is favorable after twenty-four hours.

Fat embolism is due to the crushing of the bone-tissue forcing fat into the veins in the bones. The writer's clinical experience indicates the importance of refraining from crushing the bone in operations. Bergemann (Berl. klin. Woch., June 13, 1910).

Cutting injuries of bones are liable to lead to fat embolism, the veins in the bones taking up the particles of fat. Mere concussion of the bone was sufficient, however, in some cases to induce fat embolism by the lymphatic route, the lymphatics taking up the fat particles and thus passing them along into the circulation. In *lymphatic fat embolism* prompt drainage of the thoracic duct warded off danger when the operation was done at the first signs of fat embolism. Fritzsche (Deut. Zeit. f. Chir., Nov., 1910).

Cases of fat embolism are reported only when severe and when they have a fatal outcome. Most of the cases follow orthopedic operations and fractures. The view is gradually gaining ground, however, that fat embolism is a much more frequent occurrence than formerly was supposed possible. Benestad (Norsk Magazin f. Laegevidenskab, March, 1911).

The diagnosis of traumatic fat embolism is usually based on dyspnea, rise in temperature, brain disturbances and lipuria; but these symptoms are seldom all present. A retarded pulse with accelerated respira-

tion speak strongly for fat embolism (Roux). Purplish spots on the skin of the shoulders, chest, abdomen or front of the thighs were noted by Benestad in 5 cases following fracture; by others on the mucosa and conjunctiva. In the lungs fat embolism may be mistaken for pneumonia, and in the brain for shock or pressure from hemorrhage. The symptoms are seldom fulminating; as a rule in the fatal cases death does not occur for 5 or 6 hours, or days may elapse. Fat embolism may not develop until some time after the fracture—2 weeks in Groub 's case. Tanton (Jour. de Chir., Mar., 1914).

Case of the so-called cerebral form of fat embolism. Besides the direct injury of the brain, there was greater damage from the toxic action of products of metabolism. Necropsy of the previously healthy woman who had succumbed to fat embolism 10 days after a compound fracture of the bones of the right leg revealed typical uremic necrosis of the mucosa of the ileum, while nothing was found in the kidneys to indicate chronic disease. Fat was found in the capillaries of all the organs of the circulation, especially in the kidneys. Paul and Windholz (Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 38, 614, 1925).

In 2 cases of closed fractures, fat emboli were found at necropsy in virtually all the organs; heart, lungs, liver, kidney, spleen, pancreas, gastrointestinal tract, suprarenals, seminal vesicles, lymph nodes and brain. Elting and Martin (Annals of Surg., Sept., 1925).

Fat embolism after orthopedic interventions on children was due to the fact that all these patients had been operated on before, and had been kept in plaster casts for a long period. The author notes that Lorenz tries to avoid redressement operations on such children for several months after the removal of the cast. The same applies to children after poliomyelitis, who had not been walking. The fatty degeneration of the bone marrow predisposes them to fat embolism. Diet-

ing, light, cautious (!) **massage** and **passive movements** should always precede surgery in such children. M. Schwamm (Zentralbl. f. Chir., Feb. 13, 1926).

Study of 100 necropsies revealed no endogenous cause for the fat embolism—especially no nephritis. Slight traumas may be easily overlooked. Injections of camphorated oil may cause considerable accumulation of oil in the pulmonary capillaries. Weingarten (Schweizer med. Woch., Mar. 20, 1926).

**Air embolism** may not be attended with serious consequences if only small quantities of air are admitted, but sudden death is not uncommon with the entrance of large quantities. In the latter event frothy blood is found in the right heart, and air-bubbles in the branches of the pulmonary artery. Bubbles may also find their way into the capillaries of the brain and heart muscle. It should not be overlooked that gas in the blood after death may be due to *Bacillus aerogenes capsulatus*. The precise cause of death in air embolism is not positively settled, as the results of experiments upon animals are somewhat at variance with the effects observed in man. The usual explanation is that, owing to the resiliency of the contained air, the right ventricle fails to contract with sufficient force to propel the blood forward. As a consequence the left heart does not receive sufficient blood, aortic pressure is reduced, and death results. Another factor may be the sudden dilatation and paralysis of the ventricle.

There can be little doubt, as Welch remarks, that many of the cases reported as death from air embolism are based on entirely insufficient evidence. The researches of Welch and Nuttall, and later of Welch and Flexner, on the

*Bacillus aërogenes capsulatus* made it very evident that in future all reports of air embolism must show that the possible action of this gas-forming organism was excluded. Especially in cases of so-called air embolism following uterine manipulation, the evidence, in most instances, favors infection rather than the introduction of atmospheric air. Still, all doubtful cases excluded, there can be no question that the introduction of air into the veins does in some instances cause alarming symptoms and sometimes death. Editorial (Jour. Amer. Med. Assoc., April 22, 1905).

In a fatal case reported by the writer the air embolism was due to partial detachment of the placenta during the progress of the labor. The child was dead when delivered, and the mother died half an hour after the labor with all the symptoms of cardiac distress due to air embolism. A careful examination of the uterus failed to disclose a rupture. Apfelstedt (Zentralbl. f. Gynäk., Nu. 17-26, 1907).

Case in which in an attempt to produce an abortion, quinine was insufflated into the uterine cavity through a soft-rubber catheter. The woman immediately became unconscious and died about fifteen hours later. Death was ascribed to air embolism, gaining entrance by way of the uterine sinus and carried to the right side of the heart, producing a thrombus or going still further by way of the pulmonary artery to the lungs. T. H. Fleisher (Jour. Okla. State Med. Assoc., Jan., 1910).

The writer reports 2 cases of air embolism during labor. The first occurred in an apparently healthy woman, who had had one child. Her second confinement was normal in the first and second stages. She lay on her left side in a narrow bed, with a wire mattress, which was depressed in the center. She had a little chloroform during the later stages of delivery and was not turned upon her back until after the child had been born. When the uterus again contracted, the patient suddenly exclaimed that she was dying, became cyanosed,

and had a general convulsive seizure. This passed off, and attempts were made to express the placenta, followed by uterine contraction, which caused another convulsion. The following uterine contraction produced the same result, the cyanosis became permanent, and the patient's heart greatly dilated. The placenta was removed by hand and the uterus washed out with saline solution. A pint of **saline solution** was introduced into a vein in the arm, and **strychnine** given hypodermically. The patient gradually improved and ultimately recovered. In the second case, the patient was a primipara and had always been delicate. Delivery was accomplished under chloroform by forceps, the perineum being somewhat torn. After the child was born the uterine contractions produced spasm, with air hunger, and frequency and irregularity of the pulse. Attempts to express the placenta caused uterine contractions and a return of the spasms. The patient's heart became markedly dilated. The placenta was removed by hand and the uterus irrigated with **salt solution**. No further attacks occurred, and recovery followed. Campbell (Brit. Med. Jour., Oct. 22, 1910).

Various diagnostic and therapeutic procedures on the chest—puncture, irrigation of a cavity, changing tubes, introducing a probe or a rubber catheter, bismuth paste filling, decortication, thoracoscopy, fat or paraffin plombage, pneumotomy, pneumectomy—may cause complications, proved experimentally and clinically to be caused by air emboli. The clinical pictures of these air emboli need further study by ophthalmoscopic, stool and urine examinations. The best therapy is the preventive one. When an air embolus occurs, the operation should be stopped immediately; the **head** of the patient put **low**; the heart action reinforced with stimulants. **Adrenalin** injections, administered intravenously, will increase the amount of blood passing through the brain by diminishing the blood supply in the splanchnic areas. Schlaepfer (Johns Hopkins Hosp., Bull., Sept., 1922).

Arterial air embolism is the cause of the "reflex" convulsions and death observed after intrathoracic interventions. Bleeding indicates injury of a vessel and contraindicates continuation of the operation. **Stimulation** of the heart and inhalation of **oxygen** are advisable. Artificial respiration is contraindicated. Naegeli (Schweizer med. Woch., May 28, 1925).

A few small bubbles of air injected into a vein at a slow rate are apparently harmless, and the same also appears to apply to a small continuous column of air, judging from the results of the writer's experiments. In 1 experiment, 24 ounces of air was sufficient to produce the death of a bull weighing approximately 500 pounds, so that a man weighing from 140 to 154 pounds would proportionately take about 6 or 7 ounces as the lethal dose. D'Abreu (Indian Med. Gaz., Sept., 1925).

**Foreign Bodies.**—Dust particles and other substances, after entering the lung in respiration and penetrating the tissues, are borne by phagocytes to the bronchial lymph-glands, and thence, after the disintegration of the gland, into the efferent lymph-ducts and the blood-vessels. The gland may rupture into the adjacent veins. In other instances the foreign bodies penetrate into the blood-vessels. They may lodge in the liver, spleen, bone-marrow, and other structures, or, taken up by wandering cells, be discharged from the lungs, tonsils, intestinal lymphatics, or in the bile.

**TREATMENT.**—Shock is to be combated by the usual measures. The patient should be placed at rest and the circulation equalized, and, as far as possible, coexisting disorders rectified.

Efforts should be directed toward the maintenance of heat and nutrition to the structures involved; second-

ary inflammatory or septic processes should be controlled on well-established principles. Stimulants, tonics, and hematics will often be required.

**Digitalis** to sustain the heart action and its propulsive power is very useful. **Hypodermoclysis** or, better, **intravenous injections of saline solution** have been very efficient.

In embolism of arteries which can be reached, especially those of the extremities, **arteriotomy** and **removal of the embolus** often prove successful.

Case of embolism of the axillary artery consecutive to a chronic endocarditis in which gangrene of the forearm ensued, necessitating disarticulation at the shoulder, which was done after the oval flap method of Larrey. Sherwood (N. H. Lancet, Oct. 15, 1904).

Case of **removal of an embolus** from the common iliac artery, with re-establishment of circulation. In cases of aseptic embolism immediate removal by division of the artery at the line of the embolism or below it should be resorted to. These emboli produce mere mechanical obstruction, and the circulation is at once re-established by their removal. The symptoms which indicate the occlusion of a large artery are pain, ischemia of the limb, cooling of the surface, and absence of pulsation in the arterial trunk. The number of hours that may elapse before a tissue becomes incapable of restoration has not been definitely determined, but from the length of time a constrictor may be kept on a limb for the suppression of hemorrhage and the vitality of the limb restored, we know that many hours of complete suppression of the circulation is not incompatible with restoration of the life of the tissues. In the removal of septic infarcts there is little to be gained in a practical way, as they are usually multiple. Murphy (Jour. Amer. Med. Assoc., May 22, 1909).

Only aseptic cases should be operated on, while the **operation** should be quickly carried out. The subject should

be young and free from general arterial disorder, and the seat of the embolism be readily accessible. **Massage** of the involved artery has recently been productive of good results in a few cases, but its range of usefulness is limited because it must be practised within a few minutes after embolism. Mosny and Domont (Bull. de l'Acad. de méd., Dec. 10, 1911).

Case of a man who had had symptoms suggesting a tendency to aortic aneurism and been treated for syphilis, and who suddenly developed severe pain and paralysis of the right arm. At operation an embolus 4 centimeters long was found in the axillary artery just below the orifice of the inferior scapular. Successful **embolectomy** was performed through a 1½ cm. incision in the artery, complete recovery following. Sencert and Blum (Bull. de l'Acad. de méd., July 25, 1922).

**Embolectomy** in a young man with heart disease, 24 hours after the first symptoms, resulted in complete restoration of the circulation. The occluding embolus, 3 cm. long, was lodged in the right femoral artery at the origin of the profunda. Aleman (Acta Chir. Scandinavica, Mar. 21, 1925).

**Embolectomy** done 5 hours after the onset in a woman, aged 82, with heart disease and hemiplegia. The relief from pain was immediate, and gangrene was probably averted. Amputation was required later in another case and the attempted embolectomy failed in the third case. Necropsy revealed a second embolus that had escaped detection. Torell (Acta Chir. Scandinavica, May 20, 1925).

The writer adds 2 new cases to 62 he has collected from the literature, with very good results in 33 per cent. of the cases. Söderlund (Acta Chir. Scandinavica, June 30, 1925).

Case in which an embolus was removed from the axillary artery in a man with a failing heart. The incision of the artery and extraction of the embolus under local anesthesia brought complete restoration of the circula-

tion, demonstrated by the arterial pressure and the oscillogram findings. Lian and Moure (Presse méd., Sept. 23, 1925).

Under local anesthesia the writer removed an embolus about ¾ inch (22 mm.) long and weighing 27 grains (1.8 Gm.) from the common femoral artery of a man, aged 65. The embolus was lodged at the bifurcation of the common femoral and for ¾ inch (19 mm.) above it. The result was a perfect one in every way. MacDougall (Can. Med. Assoc. Jour., Mar., 1926).

Even the **pulmonary artery** should be **opened** in an otherwise doomed patient and **Trendelenburg's technique** employed, when the conditions are favorable for operation. The thorax is opened by a transverse incision over the second rib and a vertical incision made over the left sternal border. The triangular flap thus obtained is pulled back and a piece 10 to 12 cm. long of the second rib next to the sternum resected. If more than forty-five seconds are needed to compress and open the artery, it may be clamped laterally, the compression loosened and the blood-stream let through, and again compressed, etc., and the search for emboli continued. In most cases fifteen minutes are available. The embolus can be extracted through a very small opening in the artery.

Of 878 fatalities among the 9727 patients in Korte's surgical service at Berlin during the last four years, 22 of the deaths occurred suddenly and the symptoms indicated pulmonary embolism. The Trendelenburg operation is indicated when the conditions are favorable for immediate operation. In 10 of the cases the syndrome of the embolism persisted from ten minutes to three hours before the fatal termination. Autopsy revealed embolism in 6 and conditions would have been favor-

able for operative intervention in 5 cases. In 4 others the assumed embolism did not exist; these 4 patients were about 50 and 70, and were being treated for a broken arm or femur or ovarian cyst, with no threatening symptoms of heart trouble. A syndrome characteristic of pulmonary embolism suddenly developed in the midst of apparently complete well-being, and death followed in from ten to thirty minutes and autopsy disclosed merely brown atrophy or fatty degeneration of the heart. The writer advocates, in case of the onset of the embolism syndrome, **morphine** to tranquilize the respiration, then a preparation of **digitalis** injected into a vein while all is made ready for an **operation**, which follows if these measures fail to improve, unless contraindicated by general condition. Busch (Deut. med. Woch., July 22, 1909).

The writer found, by numerous experiments on the cadaver, that **Trendelenburg's operation** to expose the **pulmonary artery** to remove an embolus is entirely practicable from the anatomical standpoint, although none of the 5 patients thus operated on was permanently cured. In 55 cases of embolus in the pulmonary artery which he had encountered during the last 6000 necropsies, the embolism followed operations on the trunk or legs in 6 of the 35 cases of which the details are known; it followed injuries of the legs in 3 others, varicose disturbances in the legs in 7, anemia and cachexia in 8, and it occurred with a heart defect in 3. In only 6 cases was the diagnosis of pulmonary embolism made during life, and in these cases the embolism proved rapidly fatal. In all the others there was an interval of from half an hour to forty-eight hours between the onset of the symptoms of embolism and the fatal termination. An interval of from three to six hours was the rule, and it is probable that the embolus gradually increased in size or that the embolism occurred in waves. This is evidenced by the transient improvement under **camphor**, and the discovery in the smaller arteries at necropsy of minute

emboli evidently older than the big one that proved fatal. The data show thus that the diagnosed embolism proved too rapidly fatal for any operative intervention, and that in the cases with a sufficiently long interval for operative interference to have been successful, the nature of the disturbances had not been recognized. The embolus was generally located in the main trunk of the artery or one of its chief branches, and from the pathologic-anatomic standpoint might easily have been removed. The great difficulty therefore in the way of successful operative treatment of pulmonary embolism is the failure to recognize it in time. Bloody sputum at the beginning of the disturbances is an almost constant symptom. Ritzmann (Berl. klin. Woch., July 17, 1911).

In fat embolism of bone surgery the writer advises a complete stoppage of the circulation during and for a short time after the operation. The tourniquet can be left on for  $\frac{1}{2}$  hour at a time. Ryerson (Jour. Amer. Med. Assoc., Aug. 26, 1916).

In air and fat embolisms the intravenous injection of warm **saline solution** supplemented by **hypodermoclysis** has been found very effective. The explanation of this action is that the fat and air globules are broken up and washed along.

In his experimental experiences with air embolism, the writer found that the heart was unable to contract over air as the valves are meant to act on fluids and not on air. After the heart action had ceased after injection of air in the jugular vein, he was able to revive it again by direct injection of 0.5 per cent. **saline solution** directly into the right ventricle. Recent publications have shown that these facts may be employed in the saving of life. Schantz, for example, has recently reported good results in cases of fat emboli, from subcutaneous and intravenous infusions of saline solutions. L. von Lesser (Zentralbl. f. Chir., Feb. 26, 1910).

[In view of the fact that death practically always occurs in embolism in important

vessels which cannot be reached, **saline solution** should be introduced intravenously in *all* forms of embolism. Duncan and Illman (New York Medical Journal, Dec. 21, 1907) showed that mixing of the body juices with blood was the predominating factor in the production of thrombi portions of which may constitute emboli. If now we recall that the body processes contain coagulating ferment and other substances capable of promoting coagulation, it will be seen that by rapidly increasing the osmotic properties of the blood, as is done with saline solution, and thereby facilitating the passage of detritus and broken-up emboli into the lymphatic system, much will have been done to save a given case. Ed.]

Much can be done to prevent the formation of embolisms. This feature is so completely and satisfactorily covered in a paper by Hugh Crouse (Surgery, Gynecology, and Obstetrics, Dec., 1909) that the following quotation is borrowed therefrom, even though it refers to both thrombosis and embolism:—

"In general the treatment of the thrombi and emboli should be prophylactic, if possible. In *Archiv für Gyn.*, 1908, vol. lvi, page 218, Singer says that thrombi are indicated in surgical cases by a pulse acceleration, unaccompanied by fever, several days before edema and cord-like vessels occur, and that the pulse rate remains high after the temperature returns to normal. Wyder, Richter, and Muhler concur in this opinion, which is opposed by Clarke. Richter (*Arch. für Gyn.*, vol. lxxiv, page 1) says that in 63 per cent. of his cases the pulse rate warned him of the thrombotic development, and that in 34 per cent. he had doubt because of the synchronous fever. Wyder says he no longer undertakes a serious gynecological operation, where edema and a high pulse rate or other signs of a recent

thrombi are present provided the general condition sanctions operative postponement. Tabor Johnson says, in operating, one should protect the wound from injury by retractors, avoid roughness, much hemorrhage, retain patient in bed longer, and aid venous return by elevating the foot of the bed immediately after operation. Boise advocates a careful examination of the heart in all contemplated operative cases, and says: 'If the area of dullness is somewhat increased, if the first sound is disproportionately weak, if after exertion the pulse rate is greatly increased, due allowance being made for existing anemia, if there is a history of chronic exhausting disease, we may justly diagnose heart degeneration, whether we detect any atheroma of the peripheral arteries or not; and, if coupled with these points, a blood test shows an excess of calcium salts with chronic anemia, we are justified in taking all possible precautions against the occurrence of emboli.' Krusen advocates blood test for calcium salt excess, for leucocytosis, and the presence of blood-plates. If an excess of calcium salts be found, Wright and Knapp, seconded by Duncan and Illman, Boise and Krusen advocate the use of 36 grains—2.3 Gm.—of **citric acid, t. i. d.**; **alcohol** and large quantities of water. Richards advocates **tobacco smoking**. Howard, **alcohol, oxygen, liquid, and fruit juices**. Mayos, Murphy, Ries, Boldt, Chanler, Gordon, Currier, and Brothers advocate as a prophylactic agent the **early getting up of the patient**, upon the theory that the heart contractions are less vigorous in a recumbent posture; that the residual blood from insufficient ventricular



action is peculiarly liable to coagulation. All of which is in part avoided by the upright position and physical exertion. Boshier says the treatment of the thrombophlebitis is largely negative, consists of **rests, elevation, and cotton bandaging**. Patient not to be allowed to make much muscular effort for some time, when it does occur, until after the complete subsidence of all local symptoms. Avoid digitalis; recommends the wearing of **elastic stockings** for quite a time."

[Very few cases of embolism would occur were **saline solution enteroclysis** used more frequently, after cleaning out the intestine. That deficient osmosis has much to do with the pathogenesis of this condition is emphasized by many physiological and clinical facts. EDITORS.]

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**EMETINE** is an alkaloid obtained from *Cephaelis ipccacuanha* (ipecac). Its chemical formula is  $C_{14}H_{18}(CH_3)NO_2$ , and it is a methyl derivative of cephaeline, another alkaloid found in the same plant. It is chiefly employed as emetine hydrochloride, which occurs as a white, crystalline powder, soluble in water and alcohol; less often as the hydrobromide, which is less soluble, at least 2 c.c. of water being required to dissolve a full dose of the salt (Rogers).

The term emetine is sometimes also taken—and until the work of Paul and Cownley in 1901 was taken exclusively—to signify a mixture of the alkaloids of ipecac, viz., cephaeline, emetine, and psychotrine, which formerly were not clearly distinguished. This mixture of alkaloids occurs as an amorphous, whitish powder, which has a slightly bitter, acrid taste, darkens on exposure, and

is only very slightly soluble in water, though more soluble in ether and especially in alcohol and chloroform.

#### PREPARATIONS AND DOSE.

—The hydrochloride or hydrobromide of the true alkaloid emetine may be given hypodermically in amebic dysentery in doses of  $\frac{1}{3}$  to  $\frac{2}{3}$  grain (0.02 to 0.04 Gm.). The expectorant dose of emetine hydrochloride is  $\frac{1}{12}$  to  $\frac{1}{6}$  grain (0.005 to 0.01 Gm.). A solution of emetine can be safely boiled for a short time, but it is probably best to boil the water first and subsequently dissolve the drug in it. Rogers found that emetine hydrochloride could be given intravenously in full doses without causing depression. Emetine is official as *Emetinae hydrochloridum*, U. S. P.

The alkaloidal mixture "emetine" is emetic in doses of  $\frac{1}{12}$  to  $\frac{1}{6}$  grain (0.005 to 0.01 Gm.) and its dose as an expectorant is  $\frac{1}{60}$  to  $\frac{1}{30}$  grain (0.001 to 0.002 Gm.).

#### PHYSIOLOGICAL ACTION.—

The mixed "emetine" is possessed of strong local irritant properties, and, when ingested, produces an abundant flow of saliva, owing to its bitter, acrid taste, followed by nausea and vomiting similar to that brought on by the whole drug ipecac. Like most other emetic drugs, "emetine" in small doses tends to increase the secretions of the tracheal and bronchial mucous membrane and induce perspiration. It is said to stimulate the liver. Administered hypodermically in large doses it causes not only vomiting, but also later diarrhea, which may be accompanied by so much irritation of the intestinal tract that blood appears in the stools. Albuminuria, cardiac depression, edema of the lungs, collapse and death are

the ultimate effects of poisonous doses. Large doses directly depress the heart, though small, therapeutic doses produce no evident action of this nature beyond an occasional reduction of the tension of the pulse. The drug is said, by reason of the cephaëline contained in it, to have a tendency to dissolve the red corpuscles when injected intravenously.

The true alkaloid emetine is much weaker as an emetic than cephaëline (Lowin), and is therefore, for purposes in which the emetic action is not desired, superior to the mixture "emetine," which contains cephaëline. It is an irritant to mucous membranes, like cephaëline, but this does not preclude its hypodermic use. It is a better expectorant, according to Lowin, than the allied alkaloid, cephaëline, and is less likely to irritate the kidneys. Experimentally, it has proven more depressing to the heart than cephaëline, though Rogers has found it practicable to give doses as large as 1 grain (0.06) hypodermically or intravenously in man without causing circulatory depression.

The subcutaneous injection of emetine and its salts almost invariably gives rise to severe local pain and tenderness, followed or accompanied by redness, swelling and deep induration which often makes muscular movement agonizing. If the solutions are injected deeply intramuscularly into the deltoids or gluteals all pain is avoided, while occasionally there is some slight tenderness for 24 hours at the site of injection. The injections can be given into alternate arms daily without any difficulty, the same site being used repeatedly at intervals of 48 hours. P. Figdor (*Lancet*, Aug. 18, 1917).

Maurel, injecting emetine hydrochloride into frogs, observed a con-

traction of the vessels in their interdigital webs and concluded that the substance is a vasoconstrictor. In the congestive zone surrounding a wound he found that it overcame vascular dilatation and reduced the degree of inflammation. This accounts, according to Maurel, for the results obtained clinically with ipecac in affections accompanied by congestion, notably in the digestive and respiratory systems. The same fact might also explain the well-known paradoxical antemetic effect of small doses of ipecac.

In entamebiasis emetine acts only through the circulation, and can influence only entamebas in the tissues. When given by mouth, even, it failed to attack amebas in the lumen of the gut. Relapses are due to survival of entamebas through encystment in the walls of the intestine. Lyons (*Amer. Jour. Med. Sci.*, July, 1915).

Emetine depresses and may eventually paralyze the heart; it is a powerful gastro-intestinal irritant, given either by mouth or subcutaneously; it causes definite derangement of metabolism, characterized by an increase in nitrogen loss and acidosis; while in normal persons who receive moderate doses these effects may not be of importance, in pathological states of the circulation, intestinal tract or metabolism, they may be a definite source of danger. Pellini and Wallace (*Amer. Jour. Med. Sci.*, Sept., 1916).

In excessive doses emetine depresses both the central nervous system and the heart. Death, where it occurs, takes place from respiratory arrest.

Several instances in which the prolonged use of emetine in apparently harmless doses led to toxic symptoms. In cats and rabbits repeated administration of subtoxic doses invariably led to cumulation with diarrhea, lethargy, somnolence, and even

coma. *Post mortem* the animals showed intestinal irritation with lesions in the kidneys and liver. Use of emetine beyond absolute needs is unwise. H. H. Dale (Brit. Med. Jour., Dec. 18, 1915).

In the treatment of 142 cases of end-amebic dysentery emetine hydrochloride gave rise to toxic effects somewhat analogous to those of salvarsan in syphilis. In the 2 fatal cases there was (1) inability to swallow after food had reached the esophagus, (2) hepatization of the lungs, and (3) rapid and uncontrolled action of the heart. Both patients showed, at first, a general motor weakness, with a tendency for the head to fall forward. One case showed decided cardiac signs. These cases had received in all  $23\frac{1}{2}$  and 25 grains (1.52 to 1.62 Gm.). In 5 other cases similar untoward symptoms disappeared promptly upon withdrawal. Johnson and Murphy (Military Surgeon, Jan., 1917).

Experiments on dogs showed that emetine hydrochloride gave rise to congestion and slight parenchymatous degeneration of the kidneys. While in one dog the drug produced hemorrhages at the sites of injection and between the layers of the renal capsule, and at the site of injection in another dog, in no case did its irritant action extend to the parenchyma of the kidneys, although it was administered in a quantity that, when injected daily, eventually caused the death of the animals. De la Paz and Montenegro (Philippine Jour. of Sci., Jan., 1918).

Injecting large doses of emetine hydrochloride into animals, the writer observed evidences of its excretion into the alimentary tract, consisting of diffuse inflammation of the intestinal mucosa, mucopurulent discharge, areas of hemorrhage, and even ulceration. Hemorrhages were also found in the lymph-nodes, spleen, and kidneys. Peripheral neuritis, weakened heart action, and fall of blood-pressure were also witnessed. Clinically, the toxic and cumulative properties of the drug should be borne in mind. One grain

(0.06 Gm.) subcutaneously every day for 12 days will cure most cases of **amebic dysentery**. Chopra and Ghosh (Indian Med. Gaz., July, 1922).

A fatal case of polyneuritis following daily injections of 0.06 to 0.09 Gm. of emetine for about 2 weeks in a woman of 37 was observed by the writer. The total of emetine given was 1.05 Gm. (16 grains). A week later the nerves of the extremities and vagi became affected, the pulse rate rose to 140, and signs of bulbar involvement ultimately appeared. Soca (Bull. Soc. méd. des hôp. de Paris, May 18, 1922).

**THERAPEUTICS.**—The mixture of alkaloids incorrectly termed "emetine" is rarely employed, as it has no advantage as an expectorant or emetic over the ordinary preparations of ipecac and is far more costly. Very small doses can be used, however, in the early stages of **bronchitis**, and the drug is said to be of value in **diarrhea** in the minute dose of  $\frac{1}{300}$  grain (0.0002 Gm.).

The true alkaloid emetine was shown by Vedder, of the United States Army, to possess a powerful destructive action on an ameba presumed to be the parasite of tropical dysentery. Further tests by Wherry and by Leonard Rogers, of Calcutta, only served to confirm this discovery, and the last-named observer, to his enduring credit, put this finding to practical use in the treatment of severe cases of **amebic dysentery**, with very gratifying results.

The writer tentatively gave two  $\frac{1}{8}$ -grain (0.021 Gm.) tablets of emetine hydrochloride by the mouth on an empty stomach, allowing no food or water for three hours before and after it, and found that the drug is generally retained, or if any vomiting occurs it is not until after several hours, when most, at any rate, of the dose has been absorbed. It is thus far

easier to administer, and much better retained, than an equivalent amount of ipecacuanha powder. Several cases of fairly mild **amebic dysentery** were cured within four days by this method, although it is less rapid and lasting in its effects than by hypodermic use; for in 1 case a relapse occurred after a few days, which was quickly cured by injections of the emetine salt. Leonard Rogers (Therap. Gaz., Dec., 1912).

Emetine is too toxic to be tolerated in any but absolutely minimal doses, according to some authors. The writer's experience, however, has been otherwise. For the past 2 years or more he has always given emetine intravenously, unless contraindicated by the age of the patient, *i.e.*, in the very young where the veins cannot be easily found, in a dose of 1 grain (0.06 Gm.) in 1 c.c. (16 minims) of distilled water on alternate days. He gave 6 to 12 injections. No ill effects followed this routine procedure. Vasavada (Indian Med. Gaz., Sept., 1924).

The superiority of emetine over the whole drug, ipecacuanha, is well shown in the following table, representing the results noted by Rogers in two series of cases—one comprising 30 patients treated with ipecac and the second including 25 patients treated with alkaloid:—

	Cases treated with ipecac.	Cases treated with emetine.
Died within three days after admission .....	4	2
Died after three days .....	7	—
Died of other disorders (heatstroke and cancrum oris) after cure of dysentery .....	—	2
Discharged in very bad condition .....	2	—
Discharged not cured .....	4	—
Discharged cured .....	13	21
Average number of days spent in hospital by cured cases .....	16.4	7.2

	Cases treated with ipecac.	Cases treated with emetine.
Average number of days before stools returned to normal .....	11.4	2.35
Average amount of drug given before stools became normal .....	406 gr.	2 gr.

The 2 grains (0.13 Gm.) of emetine referred to in the last column represent an amount of alkaloid equivalent to only 180 grains (12 Gm.) of powdered ipecacuanha—additional evidence of the high relative efficiency of emetine. The drug so rapidly kills off the amebæ that apparently moribund patients can often be brought through safely.

The blood and mucus nearly always finally disappear from the stools of an **amebic dysentery** patient within two or three days, four days being the longest period the author has met with. In bacillary dysentery, on the contrary, the drug exerts little or no effect, so that failure of injections of emetine salts to produce a very material improvement in the stools within two or three days affords very strong evidence that the disease is not amebic in origin. The amebæ disappear from the stools in twenty-four to forty-eight hours after emetine injections are begun; so the parasite should always be sought for before the drug is administered. The author has never seen any harm result from the new treatment in bacillary cases; so it can safely be used for diagnostic purposes.

Leucocytosis of from 25,000 to 50,000 or even more is common in amebic disease, and furnishes important prognostic information. Of 10 cases with such high white-corpuscle counts in which ipecacuanha was given, only 2 recovered, while 4 died in the hospital and 4 were taken away uncured, 3 in a bad condition. On the other hand, under the emetine treatment 4 out of 5 similar cases

were rapidly cured, the one fatal case showing a count of 61,750 leucocytes, and dying in less than twenty-four hours after admission. Leonard Rogers (Therap. Gaz., Dec., 1912).

Case of **amebic dysentery** of over a year's standing and suffering from recurrent attacks every two or three months. In a period of eight days the patient was given 0.3 Gm. (5 grains) of emetine hydrochloride subcutaneously; on each of the two succeeding days he was given a rectal injection of 0.12 Gm. (2 grains) each; finally he received one more subcutaneous injection of 0.06 Gm. (1 grain). Under this treatment the number of stools *per diem* fell from 16 to 2. A few amebæ could, however, still be found. Dufour and Thiers (Soc. méd. des hôp. de Paris, April 11, 1913).

Case of a man, aged 46, who had been suffering from **amebic dysentery** for five years, having had an hepatic abscess, which was relieved by operation, and who had finally become reduced to a state bordering on cachexia. Twelve to fourteen stools, containing mucus and blood, were passed daily, and there was an eosinophilia of 10 per cent. Emetine hydrochloride was given in the dose of 0.04 Gm. ( $\frac{2}{5}$  grain) once daily for a week. Abdominal pain disappeared, and the stools were reduced to 4 and became free of amebæ. The eosinophilia, however, persisted and during the succeeding nine days the stools increased to eight or ten, with blood, mucus and amebæ; abdominal tenderness returned, and the previous subjective improvement disappeared. More energetic treatment was then given, 0.08 Gm. ( $1\frac{1}{4}$  grain) of emetine being injected daily for a week, then 0.04 Gm. ( $\frac{2}{5}$  grain) for four days more. By the time the last injection had been given there was but one pasty stool a day, the amebæ and eosinophilia had disappeared and considerable subjective betterment had occurred, though the patient's appearance remained practically the same and no gain in weight had been

noted. The outstanding features of the case were the length of treatment required and the amount of drug injected—1 Gm. ( $15\frac{1}{2}$  grains),—which was well borne. E. Job and L. Lévy.

Another author refers to the case of a man who had contracted **amebic dysentery** in Morocco, and upon his return to France had been passing seven or eight stools daily. These, though very soft, were not of the dysenteric type, being free of bloody mucus and of amebæ. There was no colic or tenesmus, and the condition was undoubtedly due to a chronic enteritis. Emetine treatment gave no result, showing that the remedy cannot be counted on to relieve non-amebic intestinal disorders, even where these follow amebiasis. Dopfer (Soc. méd. des hôp. de Paris, May, 1913).

In *pregnant and menstruating women* a  $\frac{1}{2}$  grain (0.03 Gm.) daily dose of emetine is the maximum safe amount. Even the effect of these doses should be carefully watched, and no more injected than is required to kill the amebæ in the stools, all question of a complete cure being set aside until after delivery. It appears to be advisable not to give emetine during menstruation. Chalmers and Papatheodorou (Jour. of Trop. Med. and Hygiene, July 15, 1915).

An emulsion of *emetine bismuth iodide* in liquid paraffin gives much better clinical results than salol-coated pills. Of 63 cases given a 12 days' course of 36 grains (2.3 Gm.), only 12.7 per cent. relapsed, as against 45.1 per cent. after the pills in 26 cases. Injections of emetine hydrochloride proved very useful in cases where the preceding treatment could not be tolerated, 3 out of 5 cases being cured by 12 1-grain (0.06 Gm.) injections. Juppés (Jour. Roy. Army Med. Corps, June, 1921).

The beneficial effect of emetine in amebiasis is pronounced and prompt. That the amebæ may be all killed by emetine so that no relapse will occur, has not been established, but

Rogers observed that in patients who died for any reason (gangrene of the cecum; numerous small liver abscesses) after emetine treatment, no amebæ whatever could be detected in the intestines or liver.

A very severe attack of **amebic dysentery** cleared up as a result of two injections of  $\frac{1}{2}$  grain (0.032 Gm.) of emetine hydrochloride on each of three successive days. The patient returned three weeks after leaving hospital suffering from diarrhea, but without amebæ in the stools, and died in three days, left basal pneumonia being found *post mortem*. The upper half of the large bowel was distended and its wall greatly thinned in places and adherent to surrounding structures, while its mucous membrane showed extensive thin scars of healed ulcers, but no recent lesions, and the liver contained a small, encysted abscess; also free from amebæ. Thus three days' emetine treatment had brought about healing of very extensive amebic ulcers and had also sterilized and led to the encystment of a liver abscess. A second patient was apparently cured of a chronic amebic dysentery by 1-grain (0.065 Gm.) doses on three successive days, but returned four weeks later with severe dysentery and died the next day, no amebæ having been found in the stools on his second admission. *Post mortem*, extensive healed scars of amebic dysentery were found in the upper part of his large intestine, and typical lesions of acute bacillary dysentery in the lower half, from which cultures of Shiga's bacillus were obtained. These two apparent relapses furnish strong evidence that the new method can completely sterilize the body as far as pathogenic amebæ are concerned. Leonard Rogers (Therap. Gaz., Dec., 1912).

In **amebic hepatitis** the emetine treatment has proven nearly as great an advance as in amebic dysentery. Injected in the same doses as in the latter condition, emetine will remove

the pain of acute hepatitis in a single day, reduce the fever in a few days, and where abscess formation has not yet taken place, bring about subsidence of the leucocytosis (Rogers). Several French observers have fully confirmed the statements of Rogers concerning the benefit of emetine in this condition.

Report of cases of **amebic liver abscess** treated by aspiration and injection of emetine into the cavity, with uniformly excellent results and the complete avoidance of secondary pyogenic affection of the cavity, which is the common result of open drainage. Leonard Rogers (Brit. Med. Jour., Aug. 24, 1912).

Where leucocytosis in **amebic hepatitis** persists for some time after the pain and fever have subsided under emetine, it is highly probable that an hepatic abscess is present, which had formed before the treatment was begun. In that case it is usually only necessary to remove the pus by aspiration, and to inject 1 grain (0.065 Gm.) of emetine hydrochloride dissolved in about 1 ounce (30 c.c.) of water into the abscess cavity through the aspiration cannula before withdrawing it and sealing the puncture with collodion. If a full course of emetine has not already been given,  $\frac{1}{2}$  grain (0.032 Gm.) should be injected subcutaneously twice a day for three days, commencing from the day after the aspiration. The pus withdrawn should be examined by culture for bacteria, and if it proves sterile it is highly probable that nothing further will be required, for the amebæ having all been killed by the emetine, the remains of the abscess will encyst. If the abscess is a very large one a second aspiration may be required after a week or ten days.

Where secondary extensive coccal infection has taken place the abscess must be opened and drained.

In 1 case in which the pain and fever of a very acute hepatitis sub-

sided under emetine injections, but leucocytosis persisted, 10 ounces of pus were removed by simple aspiration, no more emetine being used, and complete recovery ensued.

Thus it appears quite probable that in the large number of amebic liver abscesses which are free from secondary bacterial infection—85 per cent. of the whole in the author's Calcutta experience—incision and drainage will not in future be often required. Leonard Rogers (Therap. Gaz., Dec., 1912).

Case presenting a large **hepatic abscess**, which had developed some months after an attack of diarrhea devoid of any special features. Upon incision a liter of sterile pus, containing numerous amebæ, was evacuated. The temperature fell, but an abundant purulent and hemorrhagic discharge took place along the drain. Five days after the operation, 0.04 Gm. ( $\frac{1}{2}$  gr.) of emetine was injected under the skin, and on the next day 0.02 Gm. ( $\frac{1}{4}$  grain) in 40 c.c. of water was injected into the abscess cavity.

Finally, on the two succeeding days, another hypodermic injection of 0.04 Gm. was given. After the first injection the pus was already less blood-stained; after the third it contained no more blood and was much less in amount; four days after the last injection, it had entirely ceased and the temperature was normal. A. Chauffard (Soc. méd. des hôp. de Paris, March 14, 1913).

Although evidence is convincing that emetine is the most effective drug known in the treatment of **amebic dysentery** (*q.v.*, this volume), it is apparent it is not nearly so effective when dealing with the cryptic or latent cases, as stated in American Medicine for March, 1917. These are the carriers in the true sense of the term, and the treatment of entamebiasis by British physicians has been largely concerned with the problem of freeing the chronic "carriers" from their infection. Cysts will disappear in many cases only to return; they will persist despite the emetine treat-

ment. H. H. Dale in the London Lancet (July 29, 1916) stated that the relative failure of hypodermic treatment with emetine in cystic conditions may be explained by the entamebæ being more or less completely shut off from the circulation and tissue fluids of the patient. Low, who, in conjunction with Clifford Dobell, had been employing **emetine bismuth iodide**, stated in the London Lancet (August 19, 1916) that they were convinced that emetine bismuth iodide is far more efficacious than emetine hydrochloride given hypodermically in removing the cysts from the feces of chronic carriers. EDITORS.

*Intravenous* administration of emetine in amebic dysentery has been practised with satisfactory results by a number of clinical observers in different countries. The writer reports 11 personal cases in which this route of administration was availed of. Tolerance of the drug thus given seems proven. A boy of 12, dysenteric for two months, was given 0.21 Gm. (3 grains) of emetine intravenously in five days. A complete, permanent cure resulted, without any untoward effects. Similarly, entire tolerance was noted in all the author's other cases, even when 0.28 Gm. (4½ grains) was given in five days. C. J. Bello (Observ. y Notas, Jan., 1919).

In the treatment of **hepatic abscess** emetine should only be used as an adjuvant to aspiration. Its rapid effect in acute amebic hepatitis is probably due to its action upon the amebæ themselves, and the fact that none of these organisms was found in the liver pus after evacuation in the 2 cases reported may be also attributed to the drug. There are no grounds, however, for the belief that, under ordinary circumstances, the administration of this drug in any way hastens or affects the absorption of pus which has already been formed within the liver. Manson-Bahr and Morris (Lancet, Jan. 9, 1926).

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tient from the primary condition. In cases of cardiac asthma and angina pectoris it may also occur. The area of pulmonary resonance is increased and numerous small, diffuse, musical râles heard. Thus, pressure on the vagi by enlarged glands may give rise to a similar condition.

(b) *Compensatory Emphysema*.—This is limited to a single small focus or may be widespread, even involving an entire lung, dependent upon the size and nature of the provocative lesion. If any part of the lung area does not fully expand during inspiration, some other portion of the lung will overdistend, or in time the chest wall will sink in order to fill in the space thus created. At first this is a physiological process, but in time atrophy of the alveolar walls takes place; contiguous air-cells fuse and fibrous tissue proliferation ensues. Partial or complete arrest of tuberculous foci or cavities, pleural adhesions and cirrhosis of the lung, all give rise to this condition; likewise pleurisy with effusion, especially if of long standing; also pneumothorax. In proportion to the extent of pulmonary disablement, emphysema arises, so that an entire lung and even part of the second may become involved.

(c) *Hypertrophic Emphysema*.—This condition, known also as idiopathic or substantive emphysema, was called by Sir Wm. Jenner large-lunged emphysema. The term hypertrophic is really a misnomer, as there is a diminished and not an increased functional activity. Clinically the disease is easy of recognition. The thorax is voluminous, due to the pulmonary distention; and dyspnea and especially cyanosis are, sooner or later, very pronounced.

**MORBID ANATOMY.**—In interlobular emphysema more than in any other form, heredity plays a part; it is probable that some subtle tissue change pre-exists, probably a congenitally low grade of elastic tissue. In consequence, overdistention rapidly manifests itself, whatever the cause or even without apparent cause.

When the thorax is opened it will be noted that the costal cartilages are calcified, and even in children this is apt to be the case. According to Freund, this primary change in the cartilages brings about a rigidly dilated chest with a secondary large-lunged emphysema. The lungs do not collapse even when removed from the body. They are pale (pulmonary albinism of Virchow), due to absence of pigment in parts; soft, downy, non-crepitant, and pit on pressure. In some instances the lobules are circumscribed by pigment. Distended air-vesicles may be seen beneath the pleura, varying in size, the largest along the free margins of the lungs. An inflated lung, dried and sectioned, will show these to consist of intercommunicating cavities, dilated alveoli, with atrophic septa and vessels and fibrous tissue. The lung looks bloodless and is dry, unless a hypostasis or pulmonary edema has occurred at the bases, due to cardiac insufficiency. The bronchial tubes are the seat of chronic changes, thickening and swelling of the mucosa of the larger tubes, with at most but a moderate bronchiectasis of the smaller tubes, if at all, except in cases of interstitial pneumonitis—pulmonary cirrhosis—where the peribronchial fibrosis invites a more marked bronchiectasis. Mucopurulent secretion is found in the bronchi. Pleural ad-

lesions are the exception. Rupture of dilated vesicles predisposes to pneumothorax; but if the pleura remains intact, interlobular emphysema results.

Owing in part to pressure and in part to stretching exerted by dilated air-cells, and in some measure to fibrous tissue proliferation and contraction, the pulmonary and bronchial vessels are narrowed even to obliteration, and lymphatic circulation is likewise impaired. This necessarily increases the vulnerability of the pulmonary tissue and increases the tendency to bronchitis and pulmonary inflammations.

The right heart feels the strain, the right ventricle and auricle become hypertrophied and dilated, the tricuspid orifice widens, the venæ cavæ enlarge, and congestion of all the organs drained by them results. To a less extent the left side of the heart is involved. Owing to the great increase in volume of the lungs and the depression of the diaphragm, the heart lies lower and more horizontally than normal, the anterior face of the organ being then made up entirely of the right ventricle and auricle.

Case in which marked displacement of the heart occurred, apparently due to the rupture of some of the air vesicles of the inflamed lung allowing free air to escape into the mediastinum, from which it made its way up under the right clavicle and posteriorly over the right side. The writer was forced to the conclusion that the heart could only have been displaced by the presence of air in fairly large quantities in the mediastinum. Fleischner (*Amer. Jour. Dis. of Children*, Feb., 1921).

The mitral and tricuspid valves often become fibrotic, less often the

aortic, and the pulmonary artery is invariably the seat of atheroma, more or less marked.

The liver enlarges, is congested, indurated, "nutmeg" on section, and the hepatic veins are dilated. The kidneys are cyanotic, indurated and usually the seat of a chronic, interstitial change. The spleen dense, cyanotic, and moderately enlarged. In the stomach and intestines are present more or less evidences of catarrhal change due to chronic, passive congestion.

**SYMPTOMS.**—Pathologic changes in the lungs may be advanced before the patient is conscious of any particular abnormality. Without any apparent cause, or after an attack of bronchitis or some one of the factors previously cited, some dyspnea is noted, at first on effort. The longer the myocardium is able to compensate, the more slowly will the disease progress. Anything which interferes with the descent of the diaphragm, as over-feeding, or occupations requiring stooping or crouching, or flatus, will render the pulmonary change more apparent by increasing the dyspnea. With this are closely associated, cough and cyanosis; at first, like the dyspnea, intermittent; later, almost constant, at which time orthopnea prevails. Harsh, wheezing respiration, with prolongation of expiration, aggravated by colds and intercurrent bronchitis, and attacks of dyspnea and cough, with or without cyanosis, are the only symptoms for a variable length of time.

These symptoms are more marked in winter than summer, the winter bronchitis and cough being especially troublesome. Finally these conditions persist throughout the

year, with periodic attacks of asthma. In early life, this may go on from year to year with but little change, often two or more members of a family being affected, more often the males; but with advancing age the more frequently recurring attacks of bronchitis stamp the sufferers indelibly.

It is the strain incident to coughing that taxes the circulation and hastens decompensation. Cyanosis then becomes more or less constant, and in some cases is quite as marked as it is in congenital heart disease. It may even be quite pronounced while the patient is able to be about. One seldom sees cyanosis so striking under any other condition in one who is up and about. In poisoning by the coal-tar group a similar state of affairs exists, but with the same degree of cyanosis in heart disease the patient is orthopneic.

Observations affording direct evidence that the patients suffer from impaired ventilation of the pulmonary alveoli, with consequent high carbon dioxide content of the alveolar air, rather than from a deficient intake and absorption of oxygen. None of the cases studied showed the slightest modification of the symptoms when pure oxygen was inhaled. C. F. Hoover (Archives of Intern. Med., Jan., 1913).

The moderate anemia existing is masked by the polycythemia. In consequence of the overfilling of the venous system, the arteries are poorly filled and the pulse is small and weak. The heart is irregular, intermittent, and in the later stages the blood-pressure is low. The cervical veins distend, often filling from below, even pulsating, showing incompetent jugular valves, with dilated right heart and incompetent tricuspid orifice.

Marked epigastric pulsation occurs, due to the abnormally low and transversely situated heart.

The "epigastric pain-point" is common in pulmonary emphysema. It is usually located in the immediate vicinity of the xiphoid cartilage. Pressure upon the epigastrium increases the pain and sometimes makes it intolerable. It is frequently an early subjective phenomenon in pulmonary emphysema and was seen in five-sevenths of a series of cases of that disease. H. de Buen (*Revue de méd.*, Dec., 1905).

Case of polycythemia in a man with pneumothorax. A research on 10 old horses showed that while the blood of the normal animals gave 7,000,000 erythrocytes, there were from 8,000,000 to 14,500,000 in horses with emphysema. Van den Eeckhout and Lahaye (*C. r. Soc. de biol.*, May 1, 1925).

Hemoptysis is not uncommon, but, as in mitral stenosis, the amount of blood lost is usually small. Fatal hemoptysis is rare. Expectoration never results from the emphysema alone, but is due to the associated bronchitis, and is proportionate thereto. In the earlier stages the sputum was described by Laennec as pearly, later increasingly profuse, and mucopurulent to purulent.

Deficient aëration of the blood induces headache and drowsiness. The appetite is poor, tongue coated, bowels constipated, and flatulence and distention are not only annoying, but interfere with the action of the diaphragm and further embarrass respiration.

The physiognomy is striking. Early, the rounded shoulders, forward position of the head, thick lips, congested mucosa, barrel-shaped thorax and later, with loss of flesh, the same pose with evident embarrassment of breathing, the voluntary muscles be-

ing employed; the careworn, anxious expression; cyanosis, prominent eyes, injected veins, clubbing of fingers and toes confined to the soft tissues of those parts, prominent abdomen, epigastric pulsation, low position of liver and spleen, gastrointestinal catarrh and, in time, edema of legs, later becoming general, with effusion into the serous cavities. The course of the disease is afebrile unless pneumonia supervenes.

**Physical Signs.**—*Inspection.*—For a more or less extended period no striking physical signs can be elicited. Possibly a rather resonant note over the lungs, but eventually, though very gradually (less so in those in whom marked hereditary predisposition is a factor), all of the characteristic signs develop. The most notable is the change in shape of the thorax. This becomes rounded, the anteroposterior diameter increasing, often to a greater size than the transverse diameter. The lower portion of the chest is especially voluminous, the interspaces widened; the intercostal angle becomes more obtuse as the ribs assume a more horizontal position. The sternum acquires a forward bend from above downward, and both sternum and costal cartilages are often prominent features. The neck is short, and owing to the play of the voluntary muscles during inspiration the entire thorax is lifted during the respiratory act, while the sternal fossæ appear unduly deep. There is actually very little increase in expansion, though the effort during breathing is exaggerated. Inspiration is short while expiration is prolonged. Abdominal movement may be inverted during inspiration, the upper portion being retracted instead of distended. Dilated.

venules are commonly present over the lower thoracic region, along the line of attachment of the diaphragm. Epigastric pulsation is marked; the apical impulse feeble or absent. The cervical vessels are overfilled, prominent, and in some instances pulsate. At this stage, more or less constant, often profound cyanosis is present, increased during coughing or other effort. The spine is curved anteroposteriorly, the shoulders rounded, giving a thick set to the figure. The scapulæ tend to assume a horizontal position.

*Palpation* confirms inspection as to the character of respiratory movement, feeble or absent apex beat, forcible epigastric impulse, and, further, elicits an enfeebled vocal fremitus. With an associated bronchitis, a rhoncal fremitus may be felt.

*Percussion.*—Markedly hyper-resonant note, even tympanitic, over the entire chest, often masking cardiac dullness, unless very light and superficial percussion be practised, extending abnormally low, the distended lungs displacing the diaphragm and abdominal viscera downward, and partially obliterating liver dullness.

*Auscultation.*—Over the lungs the inspiratory note is soft, feeble, short, while the expiratory element is prolonged, often harsh, and owing to the frequency of an associated bronchitis, apt to be obscured by râles, both mucous and sibilant. All other breath sounds may be replaced by râles. Cardiac sounds are feeble, with more or less relative accentuation of second sounds except the pulmonic second, which is absolutely accentuated. In the later stages, when decompensation has set in, murmurs develop, especially that of tricuspid regurgita-

tion, though a mitral systolic is not uncommon.

**Course and Duration.**—The hypertrophic or large-lunged type of emphysema is a slowly progressive malady, often beginning during childhood, punctuated by attacks of bronchitis, recurring with gradually increasing frequency, often asthmatic attacks, death resulting from some intercurrent pulmonary disease, as lobar or lobular pneumonia or, occasionally, hemoptysis, due to ulceration of the bronchial mucosa, or progressive cardiac failure. The total duration is a matter of years, but in those in whom the disease began in childhood life is seldom prolonged beyond middle age, and death not seldom occurs in early adult life. At best, the victims are semidependent members of society, for respiratory or cardiac embarrassment, or both, preclude useful effort.

(d) *Atrophic Emphysema.*—Small-lunged emphysema, so named by Sir Wm. Jenner, is essentially a senile change, an atrophic condition, part of a general wasting process. The need of respiratory interchange is therefore lessened, and, in consequence, the restriction of pulmonary area is clinically less apparent.

These cases are characterized by bronchitis and cough, which often tends to recur solely during the fall and winter months. These symptoms, with the resulting dyspnea, may recur for years or, in some cases, they may be present constantly, but increase in severity during the fall and winter seasons. Bronchial asthma is the exception in atrophic emphysema. Venous congestion, clubbing of the fingers and toes, and cyanosis do not occur.

**Physical Signs.**—*Inspection.*—The skin is harsh, dry, wrinkled; the muscles wasted; the thorax is small, but often barrel shaped, due to shrinkage, especially lateral. As the lungs gradually occupy less space, the ribs recede and become more oblique. The upper four or five interspaces may be fairly well marked, but the lower ones are crowded by the increasing obliquity to which the lower ribs are especially liable.

Respiratory excursions are much limited; the rigid thorax moves as one piece, but the disproportion between intake and output of air is less than in the hypertrophic form. The heart is apt to be considerably hypertrophied, the apex beat displaced in proportion, less from the emphysema directly than from the vascular and renal sclerosis which are part of the picture. Epigastric pulsation is not increased, —in fact, is rarely present.

*Palpation.*—This affords confirmation of inspection and feeble or absent vocal fremitus. The blood-vessels are firm, often sclerosed and beaded.

*Percussion.*—The note is apt to be more tympanitic than that elicited in the large-lunged variety. The precordial area on light percussion will be found increased. There is no displacement downward of the abdominal viscera, nor is the liver dullness obliterated.

*Auscultation.*—Weak breath sounds with somewhat prolonged expiration. A few small, moist râles can usually be heard at the bases posteriorly, and when bronchitis is present small mucous râles dominate all other sounds. Heart sounds are usually feeble, especially the muscle element, and the pulmonic second sound is rarely accentuated very much.

**DIAGNOSIS.**—The interlobular form is rarely recognized during life. It may occur after tracheotomy, or in punctured wound of the lung, but its presence may be suspected if subcutaneous emphysema is present, or when pneumothorax develops suddenly after a violent attack of coughing or severe strain. The fine, crackling râle, said to occur in some instances, may possibly be of diagnostic value. Acute vesicular emphysema is an intercurrent affection of rapid onset, a possible complication of severe forms of cardiac asthma or stenocardia. Expiration is prolonged, numerous small râles are present, and a markedly hyper-resonant note can be elicited over the voluminous lungs.

Compensatory emphysema, a frequent sequence of pulmonary tuberculosis, may be suspected in that condition. It is worthy of note that loss of function of a more or less extensive area of lung tissue, may be followed by a true hypertrophy of the remainder, increased functional capacity resulting in the uninvolved areas. In such cases, the breath sounds are harsh, bronchovesicular. Usually, however, emphysema occurs in those portions of the lung not the seat of fibrosis or softening. In such areas, the note is hyper-resonant and the breath sounds soft and distant, with diminished fremitus. In this form, examination of the sputum for tubercle bacilli is very important.

Emphysema in the apex of the lung is most common in the chronic fibrous cases with comparatively slight tendency to destructive processes. The tuberculous focus generally develops about an inch below the apex, and consequently there is a zone of sound tissue above. Assumption of emphysema in

the apex explains the clearing up of an area of dullness without this being necessarily a sign of healing. Orszag (Berl. klin. Woch., Oct. 14, 1912).

The large- and small- lunged types are so characteristic that little remains to be said of them in a diagnostic sense. The history, chest conformation, and physical signs furnish data of most importance.

*Pneumothorax* is occasionally mistaken for hypertrophic or essential emphysema. It is unilateral, however; the affected side bulges and is almost or entirely fixed; the inter-spaces are filled out without an increase of tension; the heart is displaced to the sound side; the percussion note is tympanitic in proportion to the degree of intrapleural tension, up to a certain point, beyond which, when the tension is at the maximum, the note will be dull or even flat. Fremitus is absent over the affected side and the breath sounds are either wanting entirely or may be heard feebly, possessing a metallic, tinkling quality. The coin test may also be elicited.

Rarely, cases of *failing right heart* with pulmonary edema; large, moist râles; frothy, mucous expectoration, often bloody, may be mistaken for essential emphysema. This is most likely in cases of mitral stenosis or chronic interstitial Bright's, where dilatation has superseded hypertrophy. Of course, in the late stages of emphysema, cardiac failure is super-added and similar symptoms may result. Several days may have to elapse before the differential diagnosis is possible. Atrophic or senile emphysema seldom presents any difficulty in diagnosis.

In certain cases emphysema is only apparent, the cases being in reality

dyspneic dyspeptics, with a small thorax and a large abdomen. This may be elicited by a clinical study and radioscopy. The thorax is made smaller by the rising of the diaphragm, due to the excessive abdominal mass, which results from gas and aërophagia and the exaggerated tension of the abdominal parietes the muscular coat of which is doubled by a thick coat of fat—all such subjects being obese. This false emphysema is readily curable. Caussade and Leven (*Presse méd.*, April 13, 1912).

**ETIOLOGY.**—Emphysema occurs at any age, most commonly, however, in late adult life, especially the atrophic form, which is usually senile. The hypertrophic variety is the form most commonly met with in the young. It is most frequently met with among men, in large measure owing to their occupation and greater liability to muscular strain, exposure, etc.

As to heredity, the hypertrophic form may be spoken of as a family type, the quality of vital tissue transmitted, so to speak, being such as to predispose to emphysema. Both in this form and even more so in the atrophic form, vascular and renal degeneration (sclerosis) are common. The hypertrophic form met with in children is very apt to exist without any history of an adequate exciting cause, and even before the disease is well developed, the child lacks animation, tires readily, and manifests little desire for the more active sports of childhood. Capacity for work, though in large measure dependent upon structural differences in individuals, is not susceptible of proof, grossly or minutely, and it is this subtle difference in tissue quality, and especially in the elastic tissue, that invites in one an emphysematous condition, while another escapes.

Muscular effort is the predominating occupational factor, and even those trades involving the inhalation of dust are chiefly harmful in consequence of the associated bronchitis and cough thereby induced. Anything, therefore, which necessitates severe muscular effort, invites the possibility of emphysema, and this possibility is greatly enhanced by certain family types. Porters, stevedores, and laborers are more susceptible even than players of wind instruments. Especially liable are grinders, stonemasons, and coalminers, owing to the irritation of the bronchial tract.

In 22 players of wind instruments, and a number of other persons, there was found a tendency to overdistention of the upper part of the lungs. Diffuse chronic emphysema, however, is generally the result of disturbances in breathing caused by chronic inflammatory narrowing of the bronchi. E. Becker (*Beiträge z. Klinik der Tuberkulose*, Bd. xix, Nu. 2, 1911).

Certain diseases are apt to be followed by emphysema, as whooping-cough, chronic bronchitis, asthma, and any factor which lowers pulmonary elasticity, as chronic heart disease or advancing age. Pneumonia, pleurisy, and tuberculosis are prone to give rise to focal or circumscribed varieties of vesicular emphysema.

**Traumatic Emphysema.**—Traumatism is most apt to invite the interlobular or subpleural varieties. Rupture of the air-cells permits the escape of air into the interlobar or subpleural tissues. Injury to the lung, as in some cases of fractured rib, punctured wounds of the thorax, violent strain as in weight lifting, paroxysmal cough, and rarely during convulsions, parturition or defecation.

Emphysema as a complication during labor is rare. In a case that occurred at the Sydenham Hospital in New York, during the acute stage of labor, a swelling suddenly appeared on the right side of the neck and face. Before the completion of the labor it had extended to the root of the neck and upper part of the chest. The eye of the affected side was completely closed up. It disappeared in 10 days. Similar instances have been known to occur from excessive vomiting or paroxysms of coughing. This complication is rare; Kosmak in 1907 could collect only 77 cases in the literature since 1791. It occurs almost always in primiparæ. The prognosis is good. Siegelstein (Jour. Amer. Med. Assoc., July 22, 1911).

Two cases of extensive emphysema developing from rupture of a cavity in the lung or wound of the lung from a fractured rib. The patients suffered greatly from the general diffusion of air, threatening suffocation, until the author introduced an ordinary **puncture** needle to which a rubber tube was fastened, the outer end of the tube resting in a vessel containing an antiseptic solution. The relief was immediate, the escaping air bubbling up through the fluid and the distended tissues subsiding into place; the patients succumbed to the original or primary disease without having suffered through their emphysema. Brondi (Gaz. d. osped., Feb. 29, 1912).

Case of orbitopalpebral emphysema caused by perforation of a dental canal was observed by the writer. It is uncommon and is a result of the fracture of the nasal, lacrimal or ethmoidal bones. There is sudden swelling of the lid and adjacent tissues, with no signs of inflammation. The swelling does not pit on pressure and there is no exophthalmos. Aaron Brav (Jour. Amer. Med. Assoc., Oct. 9, 1915).

**PATHOGENESIS.**—Two theories have long prevailed concerning the pathogenesis of emphysema, viz., the inspiratory and expiratory hypothesis.

*Inspiratory Hypothesis.*—The earlier view, originally promulgated by Laennec, regarded the inspired air as the distending force, its egress being hindered by bronchial mucus or swelling of the bronchial mucosa.

Sir Wm. Gairdner, in 1850, looked upon some change in the lung, as collapse or a retrocedent tubercle, as a necessary precedent of emphysema.

*Expiratory Hypothesis.*—Mendelssohn, in 1845, was the first to claim that forced expiration is the chief factor in the production of emphysema. Not cognizant of this at the time, Sir Wm. Jenner, in 1857, announced the same view, but in his article in Reynolds's "System of Medicine," he gives due credit and further states that "Mendelssohn's paper was unknown in this country (England), and rarely, if ever, referred to abroad till Biemer's article appeared in 1867. Jenner states that "The lung during expiration is compressed at different parts with different degrees of force. The parietes of the thorax in consequence of their anatomical constitution, yield to the same force at different parts with various degrees of facility.

"The chosen seats of emphysema are exactly those parts of the lung which are the least compressed during expiration and which are situated under those parts of the thoracic parietes that give way the most readily before pressure." Any extra effort made at the end of inspiration, when pulmonary tension is at its height, especially when the glottis is closed, forces the air centripetally, and the peripheral portions of the lung least supported suffer most; hence we find the lungs most apt to be emphysema-



tous at the apices, and along the anterior margins of the lower lobes and the margins of the extreme base, this latter, especially on the left side, as the stomach area is less resistant than the region of the right lobe of the liver.

Hence the cough, especially resulting from bronchitis, and repeated muscular strain of any kind, increase intrapulmonary tension. If the quality of tissue be good, no harm may follow unless the exciting factor is operative over a considerable period of time.

It is thus quite comprehensive that an acute vesicular emphysema or even interlobular emphysema may occur, recovery being proportionate, especially to the inherent quality of the elastic and muscular tissue. In asthma the changes are more gradual. Bronchial obstruction causes at the same time increase in expiratory effort and an increase in the quantity of residual air. Likewise laryngeal obstruction, be the cause what it may. Necessarily, in time, compression and distortion results in further obstruction of the bronchi and more or less vascular obstruction, and thus a lowered nutritional state results, predisposing the lung to a further yielding.

**TREATMENT.**—Emphysema as a disease entity is not known to the laity. It is not the emphysema as such for which the patient seeks relief, but the associated bronchitis which is an inevitable phase of the well-developed form. Just as is the case in the earlier stages of cardiac decompensation, so in emphysema, the shortness of breath (at first only on effort) does not constitute sufficient ground for annoyance or dis-

comfort, as in both of these conditions the individuals become more or less accustomed to it.

Good results are reported by the writers from **vaccines** in 16 subjects, mostly from 50 to 80 years old, who had a history of tuberculosis, had been suffering from bronchitis and emphysema for many years, and were troubled with increasingly frequent asthmatic attacks. The treatment was essentially a desensitization produced with Maragliano's vaccine or other vaccines prepared with killed tubercle bacilli partially or completely freed of fats. The vaccines were employed by scarification, so that only minute doses entered the system. General reactions were uncommon. A number of the patients were cured by the procedure in 36 hours; 2 of these had had asthma for 50 and 43 years. The relief lasted at least 6 months. Bonnamour and Duquaire (Lyon méd., July 25, 1922).

*In the young* who have sustained acute overdistention, as a result of spasm, whooping-cough or some laryngeal or bronchial affection, the process subsides with the recovery from the provocative factor.

In the *hypertrophic form*, even in childhood, when once thoroughly developed, or in the *atrophic form* in later life, very little is to be expected, indeed, if anything, from any plan of treatment. Some effort should be made, chiefly through regulating the life of the individual, to prevent the resultant effects upon the circulatory apparatus. More, however, may be done in a preventive way, through **change of climate or occupation**. Any effort which induces shortness of breath should be restricted as far as it is possible to do so. Unfortunately, since patients do not present themselves until some one or other of the complications or sequels of emphysema make it urgent, it is frequently

impossible to render any considerable degree of benefit.

The principle underlying therapy is the removal of residual air; consequently some form of aërotherapeutics may be employed, the patient breathing into the rarefied air. This plan has been followed by Dr. Fowler, who, however, believes that the results are not so satisfactory as the employment of what he terms **compressed air baths**. These he has used at the Brompton Hospital with considerable success. He states that breathing is greatly facilitated, while in the bath, and that capacity for exercise materially improves after a series of them have been taken; also the cough and amount of expectoration are greatly lessened. This method, however, is not generally applicable.

In 6 patients under treatment by **respiratory exercises**, first case a man of 49 had bronchitis every winter, accompanied with dyspnea and cyanosis when the patient was first seen. After 42 *séances* of respiratory therapy in the course of seven weeks the lung capacity increased from 3000 to 4000 c.c. while the dyspnea and cyanosis disappeared. The excursions of the thorax increased from 1 to 5 cm. Haus (Norsk Magazin f. Laegevidenskaben, lxii, No. 5, 1906).

The writer uses a contrivance which presses in the abdominal wall—an air-filled cushion under an inelastic band. The cushion is inflated to exert pressure just at the end of expiration; it forces up the relaxed diaphragm and the immediate relief is so marked that the patient realizes the advantages from drawing or forcing the diaphragm up as high as possible during expiration, and he learns to utilize his own forces for this. The circulation is promoted at the same time by these breathing exercises to such an extent that the general health is materially bene-

fited. Hofbauer (Wiener klin. Woch., March 28, 1912).

One of the most useful devices for this purpose is **Rossbach's chair**, which can be worked by the patient or an attendant, and affords great relief. It is of the ordinary modern type without arms and with a straight back. The seat is prolonged backward about three inches and two horizontal brackets, *B*, are attached to the top rail. These support two wooden cylinders, *A*, about three inches in diameter and as long as the back of the chair. They are placed on each side just without its outer rail. These revolve on iron pins which pass through the projection of the seat and the brackets respectively. At the bottom of each is attached a lever or wooden handle of convenient length for the patient to grasp with his arms extended. When drawn forward parallel to each other the cylinders make a partial revolution. A broad band of strong webbing (*F F'*, Fig. 2) passes across the chest of the seated patient and is attached by eyelet-holes to a row of studs, *C*, on the inner face of the two rollers; therefore, on pulling the handles forward the thorax is compressed to any extent which may be thought necessary. The bandage is divided in the middle and is fastened in front as a corset. The patient rests himself in the chair, well back, the levers are drawn outward and the belt adjusted so as to press equally over the thorax, and is fastened to rollers on either side. Extending his arms, he grasps the handles, takes a deep breath, and, as expiration commences, pulls them slowly forward; the act completed, he pushes them somewhat quickly to their first position, takes another deep breath, pulls them gently together again as far as he finds necessary, and so on. Here we have artificial respiration with an automatic operator. These movements are timed and persisted in as long as the physician may direct, fifteen times per minute for ten minutes, three times a day. This instrument equally compresses the chest. The patient can use it when once adjusted, either day or night. Any carpenter can make it at little expense. It can be used simultaneously with other forms of treatment, such as Waldenberg's cabinet, or with expectorants and cardiac tonics. EDITORS.

Patients seen in the earlier stages, even though already the subject of

some degree of bronchitis and possibly venous torpor, may be considerably aided by general **massage** and **exercises** of the character known as **setting-up exercises**, now commonly practised in classes in the various gymnasia, but equally practical if a

method of retaining the blood in the periphery. The heart grew smaller, both the arterial and venous blood-pressure dropped, etc., and patients with emphysema disturbances felt relieved as soon as their limbs were thus excluded from the general circulation. Tornay has reported similar benefit in conges-

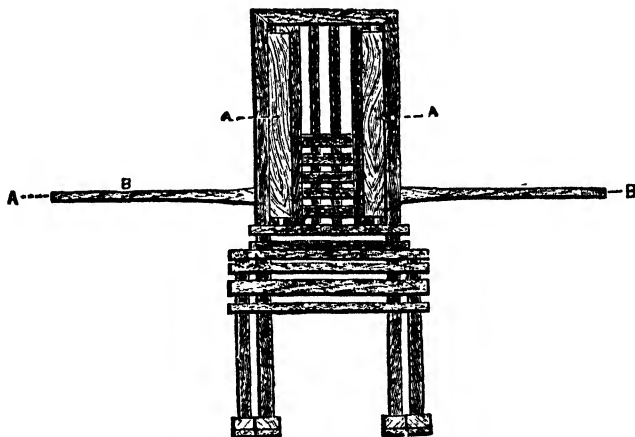


Fig. 1.—Rossbach chair, corset removed.

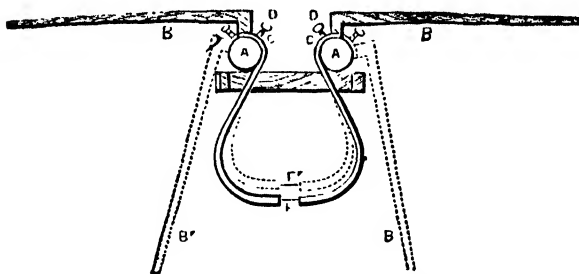


Fig. 2.—Rossbach chair, view from above, showing corset bandage  
(Illustrirte Monatsschrift f. ärztliche Polytechnik)

patient can be induced to employ them at home.

When the venous circulation is defective, throwing extra work on the right heart, with congestion in the abdominal vessels, transient benefit may often be realized by tying off the limbs as a bloodless substitute for venesection. This is proving a useful means to influence favorably acute weakness of the right and left heart manifesting itself in pulmonary edema. The writer has confirmed by extensive animal experimentation the effectual action of this

tion from cirrhosis of the liver, and Lillenstein has recently devised what he calls a "phlebostat" to accomplish this bloodless bloodletting. The writer commends this measure as a simple and harmless means to relieve extra strain on the venous heart. It can be applied with any simple **constricting band** or **tourniquet**, to both arms and legs at the same time, applying the constriction so as to arrest the venous circulation but without interfering with the arterial circulation. By this means it is possible to drain as much

as a liter of arterial blood into the limbs and hold it there. After half an hour the constricting bands are gradually loosened. The procedure can be repeated two or three times a day. Von den Velden (*Therap. Monats.*, July, 1912).

Spasmodic dyspnea, bronchitis, and cardiovascular phenomena are the three conditions which especially demand relief. The dyspnea and bronchitis almost invariably occur as associated factors, while the cardiovascular phenomena only present themselves in an urgent manner in the most advanced cases. It is to the former of these two, therefore, that our attention should be especially directed. For these it may be urged that absolute removal from all occupations, in which dust is a necessary accompaniment, is an absolute prerequisite. Change of climate is not possible to the great majority, therefore, all that remains is the use of general and rather vigorous **massage** and the practice of **gymnastic exercises** in the form of **calisthenics**.

In using the **mechanical measures** which have been employed to aid respiration in emphysema, the conditions to be dealt with are the lessened elasticity of the lung, the weakness of the respiratory muscles, and fixation of the thoracic framework. While a healthy man can exert an expiratory pressure of 100 to 150 mm. of mercury, in emphysema the figure is only 50 to 80 mm. The pressure exerted by the elasticity of a normal lung is about 18 mm. of mercury; hence the loss of this is not sufficient of itself to explain the great diminution of expiratory force, which must, therefore, be due to the other two factors. In the absence of any means of arresting or curing the degenerative changes in the lung tissue, treatment has been directed, first, to helping expiration by **pressure on the chest wall** during that phase: this may be applied with the hands, or by means

of a special instrument, or by **letting** the patient breathe out into an artificially lowered atmospheric pressure. In these methods inspiration is not affected. Secondly, artificial respiration has been carried out by apparatus devised to help both the inspiratory and the expiratory process. Thirdly, exercises have been used to increase the power of the muscles used in each phase. Fourthly, an **elastic shirt or corset** has been worn to oppose inspiration while helping expiration. In reviewing these methods the author strongly recommends the last. He uses a **vest** composed of an **elastic tissue**, exerting pressure upon the lower part of the chest; by means of buckles the pressure can be varied. The vest is worn day and night. With this instrument the chest is kept in the expiratory position, in which the muscles of inspiration act at the best advantage. The obstruction to breathing in is found to have no drawbacks. On the contrary, it is in those cases in which weakness of the inspiratory muscles is marked that the best results are obtained, and the vest can be tightened as the muscles get stronger. Wolf (*Wiener Klinik*, April, 1905).

The writer gives **iodine** and **arsenic** and has the patient exercise in a **Waldenburg apparatus**, breathing in compressed air. In one of the cases described, the lungs have returned to normal size and the expiratory force has risen from 40 to 95, while the patient has gained about 20 pounds in weight. De Renzi (*Gaz. degli ospedali*, xxviii, Nos. 30-36, 1907).

Good results obtained from **elastic webbing** around the chest in pronounced cases. In a child whose chest expansion was reduced to  $\frac{3}{4}$  of an inch, **rest** for a couple of months, with the cotton webbing, brought about complete restoration of respiratory function, the expansion increasing to  $2\frac{1}{2}$  inches. Macalister (*Liverpool Medico-Chir. Jour.*, Jan., 1914).

For the spasmodic dyspnea, the more urgent its character and the

more akin to asthma, the greater will be the need of an opiate in some form. The acute attack having subsided, it will be advisable to use **belladonna** and the **iodides**, with **strychnine** used separately owing to its incompatibility with the iodides.

Elasticity in the chest wall is the main factor to be combated in the treatment of emphysema. Of the operative measures which aim to restore this elasticity, **chondrotomy** is indicated before the condition has entailed atrophy of the muscles of respiration and severe disturbances in the circulation. (See below). **Potassium iodide** is still the best expectorant for bronchitis with emphysema. **Epinephrin** has a favorable influence in asthma, probably from the anemia it induces in the mucosa of the finer ramifications of the bronchi, thus reducing the resistance to expiration. The benefit from sweating procedures, **electric light baths**, is probably from the same mechanism. All measures are rational and useful which aid in strengthening the muscles of respiration and promoting expiration of residual air. Of special importance is the strengthening of the diaphragm. Minkowski (Therapie der Gegenwart, Feb., 1912).

**Counterirritation**, or **cupping**, during the acute phases should be resorted to, and in the intervals between the acute attacks, at which time only should the exercises be practised; effort should be made, through the medium of **iron**, **arsenic**, and **strychnine**, to improve the patient's nutrition.

Particular attention, at all times, should be given to the bowels, both with the idea of preventing tympanites, which mechanically interferes with respiration, and because the straining attendant upon constipation is liable to further damage the pulmonary structures.

The respiratory passages should be kept in an aseptic condition. The writer recommends:—

℞ *Bismuth subnitrate*,  
*Boric acid* . . . . . gr. lxxv (5 Gm.).  
*Camphor*, finely  
 powdered . . . . . gr. cl (10 Gm.).  
*Cocaine hydro-*  
*chloride* . . . . . gr.  $\frac{3}{10}$  (0.019 Gm.).  
*Menthol* . . . . . gr.  $\frac{3}{4}$  (0.048 Gm.).

Mix thoroughly. Sig.: For a snuff.

Before using the foregoing, the passages may be washed with a 3 per cent. solution of borax. The same solution, flavored with mentholated alcohol, may be used for the mouth and throat, or a good liquid dentifrice will serve.

As to internal treatment by drugs, the writer prescribes:—

℞ *Sodium arsenate*. gr.  $\frac{3}{4}$  (0.048 Gm.).  
*Potassium iodide*. gr. lxxv (5 Gm.).  
*Distilled water*.. 3x (300 c.c.).

M. Sig.: Large tablespoonful ten minutes before meals. Continue for ten days, then intermit.

For the ten days of intermission, order:—

℞ *Strychnine sul-*  
*phate* . . . . . gr.  $\frac{9}{20}$  (0.03 Gm.).  
*Distilled water*. 3x (300 c.c.).

M. Sig.: Dessertspoonful twice a day.

All treatment of pulmonary emphysema is more or less palliative, as the condition is essentially chronic. Robin (Thér. usuelle du praticien, 1911; N. Y. Med. Jour., Sept. 9, 1911).

Turpentine, terebene, cubeb, copaiba and such remedies of alleged value, where the expectoration is excessive, possess very little, if any, efficacy, at the same time having the disadvantage of greatly disturbing digestion. An occasional **blue mass pill** or a dose of **calomel** at bedtime, followed by a **saline** in the morning. In those who, for any reason, will not or can not exercise, the more or less continuous use of **fluidextract of cascara** may be employed, both for their

effect on the bowels and indirectly for their effect in improving digestive secretions. In the later stages, when cardiovascular symptoms supervene, **venesection** may be necessary, and, indeed, is sometimes absolutely demanded to relieve overdistention of the right heart. Some one of the **digitalis** group, preferably the infusion or the tincture of digitalis, may then be employed.

The writer resorted to **bleeding**, withdrawing about 250 Gm. blood, and injected **camphorated oil**, and under these measures the man of 70 was materially relieved from his sudden menacing suffocation. Galliard (Bull. de la Soc. méd. des hôp. de Paris, Oct. 19, 1917).

Surgical measures, particularly **Freund's chondrotomy** or **resection of costal cartilages** that are the seat of pathological changes which annul their elasticity and prevent the descent of the ribs, thus giving the chest the characteristic barrel-shape, are useful in some cases.

**Freund's operation** is indicated where the pathological findings are as follows: the costal cartilages are of a dirty yellow color, in a state of fibrillation and cystic, showing also calcareous deposits which cause them to become increased in size; they are hardened, brittle, and devoid of their normal elasticity. When such changes are present, the proper excursion or motion of the corresponding ribs is interfered with. The cartilages of the second and third ribs of the right side are most frequently involved, but these changes may involve all the costal cartilages. The first cartilage, however, is rarely, and then usually the last, to be involved in this disease. With the degeneration of the cartilages and the accompanying rigidity of the ribs, the sternum is forced outward and contributes eventually to the formation of the rigid barrel-shaped thorax, which retains the lung

in a continued state of distention. With the increase in the diameters of the chest, the normal function of the diaphragm is interfered with, and the muscle shows evidences of atrophy and fatty degeneration. By removing or resecting the offending cartilages, the proper functioning power of the chest may be restored; the ribs will be permitted to exercise their proper range of motion, and the proper expiratory efforts of the lungs will be facilitated. The writers found that Freund's operation is of great benefit in emphysema with a rigid, dilated condition of the thorax. Goodman and Wachsmann (Med. Rec., May 16, 1908).

**Freund's operation** done in 30 cases; in 80 per cent. the result was either a cure or an amelioration, the cure being based on the return of working capacity of the individual and the disappearance of the broncho-asthmatic phenomena. There were: Cures, 20 per cent.; improvement, 62.7 per cent.; stationary, 13.3 per cent.; deaths, 3.3 per cent. The ultimate outcome was also satisfactory. In 6 all respiratory disturbances disappeared—in 1 for 6 years and in 2 for 4 years. The operation was bilateral in 1 case and lasting improvement resulted. F. Bircher (Deut. med. Woch., Feb. 28, 1918).

Alarming cyanosis and dyspnea followed the injection of 200 c.c. of nitrogen in a man of 48 years with emphysema and tuberculous infiltration of the right upper lobe. Pulmonary congestion followed and the man died in 3 weeks. A warning is given against artificial pneumothorax in emphysema. Wulff (Berl. klin. Woch., Dec. 26, 1921).

The writer had 5 emphysema patients treated with **partial pneumothorax**. It diminished the residual air and the patients felt decidedly better. He learned the procedure is used in emphysema of horses. Schwenkenbecher attempted it once in a man but desisted, because the patient complained of severe pains. Ganter (Münch. med. Woch., Feb. 5, 1926).

It cannot be urged too strongly that routine physical examinations should be made of all patients presenting themselves for treatment, irrespective of the condition. It will often be possible to detect those morbid states which invite the development of emphysema and to recognize early stages of that disease at a time when it may be possible to be of distinct service.

W. EGBERT ROBERTSON,  
Philadelphia.

**EMPHYSEMA, SUBCUTANEOUS.**—Besides the pulmonary emphysema described above, there are others in which the spaces of connective tissue under the skin become infiltrated with air, viz., *cutaneous* or *subcutaneous emphysema*. There are besides, the artificial or false forms in which gases of microbic origin are the pathogenic agents, viz., *septic* or *gangrenous emphysema*. (See GANGRENE.) *Traumatic emphysema* and *surgical emphysema* are additional types due, as their names indicate, to traumatism or injuries and to surgical procedures, which were referred to under the preceding heading.

**SYMPTOMS.**—Subcutaneous emphysema—the only type here considered—appears as an ill-defined edematous swelling which pits under pressure, imparting to the finger a fine crackling sensation. After rupture of the lung it rarely occurs unless there is pneumothorax. The emphysema first appears at the root of the neck about the trachea and great vessels, reaching there along the bronchi, trachea, and vessels from the pleura. It also infiltrates the tissues about any wound in the parietal pleura.

After wounds of the lung there is often an infiltration of air about the external wound, and this is especially liable to occur if the wound is small or roughly sutured so that the air may, by the variations of intrathoracic pressure, be forced into the deeper tissues, but not through the skin.

**TREATMENT.**—Circumscribed subcutaneous emphysema is rarely a matter of any moment; it is usually slight in extent and quickly absorbed. It rarely ends in suppura-

tion. But if the laceration in the lung acts as a valve, pumping air into the lung with each inspiration and allowing none to escape with expiration, the emphysema may spread over all the thorax, even over the whole body, in which case the danger is from suffocation.

Half an hour after being run over by a wagon, a robust, 8-year-old boy was found to be suffering from emphysema, extending over the whole body except the palms and soles. Penis and scrotum were so puffed up as to resemble oblong rubber balls, and an attempt to hold the eyelids open with adhesive straps proved unavailing because of the tense state of the skin. The tissues under the scalp were also involved, crackling being distinctly perceived. The skin of the whole body was tense and pale. There were slight contusions on the elbow and chest. Respiration was labored. Palpation disclosed fractures of the sternum and second right rib. Three hours later the emphysema had so increased as materially to interfere with respiration; skin stretched almost to the limit of its elasticity; increasing cyanosis. On incising the chest the effect was instantaneous, as if a tense rubber ball had been pricked, and breathing immediately became deeper and slower. Two rubber drainage-tubes were inserted and left in for five days. C. G. Molin (Brooklyn Med. Jour., Oct., 1897).

A child of 8 years with Pott's disease began to cry out, became excited, and complained of severe headache. This was followed by stiffness of the neck, photophobia and obstinate constipation, and the diagnosis of tuberculous meningitis was made. Suddenly respiration became labored, Cheyne-Stokes, the eyelids and cheeks swelled up, and the eyeballs protruded. This edema gave a fine crepitation and was evidently subcutaneous emphysema. Soon both sides of the neck and the upper part of the chest were involved and the patient was comatose. She rallied somewhat for a time, but the emphysema progressed, and death took place after ten days. At the *post mortem* there was found an intrapulmonary rupture of a sub-

pleural tubercle, without perforation of the pleura. The air penetrated the interlobular tissue, and thence reached the mediastinum, neck, and face. P. Guillaume-Louis (*Arch. gén. de méd.*, Aug. 18, 1903).

The emphysema in the writer's case occurred in the face during the first stage of labor. The swelling increased and was accompanied by cyanosis during the pains. The crackling sensation of subcutaneous emphysema was found present over the swollen area, extending over the neck and right side of the face; the right palpebral fissure was reduced to a slit. Forceps were applied and the patient was delivered of a living child. Within about seven hours the emphysema was widespread. There was some pain in the chest and at the back of the neck, but the patient appeared to be little the worse. She made a good recovery, all the swelling disappearing in eight days. Stock (*Lancet*, March 16, 1912).

The treatment is **multiple incisions**. At the same time the intrathoracic pressure must be relieved by **paracentesis** or **drainage**.

Emphysema following exploratory puncture of the chest has rarely been reported. Three cases are related.

In puncturing the chest one must not forget the possible proximity of firm and unyielding lung tissue to the chest wall, and the author thinks the operation is too often undertaken with disregard of the element of danger, especially in children. When a small collection of fluid overlies a more or less consolidated lung, diagnosis by percussion and auscultation is often unsatisfactory, and **puncture** becomes imperative, **but the lung must be avoided** unless one is searching for an intrapulmonary collection of fluid. Gittings (*Arch. of Ped.*, Jan., 1908).

Case of a primipara, aged 33, who, after a prolonged labor in which delivery was effected by axis traction forceps, gave birth to a male child on Sept. 22, 1910. Although the heart was working well, artificial respiration had to be employed for about twenty minutes as the infant at first refused

to breathe, and a large quantity of liquor amnii was expressed from the mouth and nose. The following day acute edema developed over the head, thorax and scrotum. The bowels and urine were normal. On September 26th, the child, which had been crying lustily for the last twenty-four hours, suddenly became silent. The edema was then being rapidly replaced by a subcutaneous emphysema over the front and back of the head and thorax. The child could swallow well, but had complete aphonia. The breathing was slightly stridulous; there was no cough.

**Hot fomentations** were applied to the **neck**, the nostril and nasopharynx were sprayed with **normal saline solution**, and 3 m (0.18 c.c.) doses of wine of **ippecacuanha** were given every two hours. At midnight the emphysema had increased, and there was considerable dyspnea. Râles and rhonchi were heard over both lungs, the respirations were 48, and the pulse was feeble. The infant was listless and showed no desire for food. **Hot fomentations** were then applied to the **chest and back** and 20 m (1.25 c.c.) of **brandy** were given every hour, together with wine of **ippecacuanha** and **syrup of tolu and squills**. The following day, September 29, the child was better generally, and took its food well. The emphysema was less on October 1, the child could cry loudly and the emphysema had almost gone. Recovery followed. (*Brit. Jour. of Children's Dis.*, Feb., 1911).

In 2 children—18 months and 2 years of age—with mediastinal and subcutaneous emphysema, the prognosis was grave. A transverse **incision**, 5 to 6 cm. long, was made in the jugular fossa, to allow the air to escape, and the children put for a few days into an **oxygen chamber**, while keeping them somnolent with **phenobarbital-sodium**. Reimold (*Klin. Woch.*, Feb. 26, 1926). S.

**EMPHYEMA.** See PLEURISY.

**ENCEPHALITIS.** See MENINGES AND BRAIN, DISEASES OF.



**ENDOCARDIUM AND VALVES, DISEASES OF.**

—Under this head will be considered the various inflammatory disorders of the endocardium and of the cardiac valves which form part of the endocardium.

**ENDOCARDITIS.—DEFINITION.**

—Inflammation of the membrane lining the cavities of the heart. The process may be acute or chronic. The acute form is variously described as "simple," "benign," or "verrucose," and "ulcerative," "septic," or "malignant," according to the mildness or severity of the disease; but between these two forms there is in reality no dividing line. The disease attacks mainly the valves of the heart.

**ACUTE ENDOCARDITIS.**

**SYMPTOMS.**—The onset of acute endocarditis is insidious. There may be no symptoms which call especial attention to the organ affected. There may be a slight rise of temperature and some quickening, and possibly some irregularity, of the pulse. In the benign form there may be no evidence of the disease until two or three months after it has run its course, when impairment of the valves is detected. In some cases there is precordial pain, or, if the patient is a child, there may be epigastric distress, with vomiting. The pulse is of low tension, and the patient may be restless and anxious, and may prefer a somewhat recumbent to a horizontal position. Examination of the heart will disclose in most cases a murmur, usually of a blowing character, and usually systolic in time. It may accompany or replace the normal sound. Before there is an actual murmur, it may be possible to detect an impurity and prolongation of the

first sound of the heart, indicating involvement of the mitral valve. Even in the malignant form the symptoms may be masked by those of the original disease. In the severer cases sometimes there is a true chill or a succession of chills, and the fever may be either typhoidal or intermittent or remittent in its character. The patient gives evidence of great prostration. The pulse is rapid and irregular; the body bathed in profuse perspiration; the spleen enlarged and tender. There may be a rose-colored eruption upon the body; more often petechiæ are seen. The number of white corpuscles in the blood is greatly increased.

In some cases, even the worst, careful and repeated examination by competent observers may detect no cardiac murmur whatever.

The simple form may give rise to embolism in different parts of the body, and may also be complicated by pleurisy or pneumonia. The malignant form is still more apt to give rise to emboli than is the simple form, and also frequently distributes infection. In fact, scarcely any tissue is exempt from these dangers. Thus, there may be embolism of the brachial, femoral, or external iliac arteries, or of the capillaries of the skin. There may be infarctions in the spleen, causing a swelling and tenderness of that organ; in the kidneys, giving rise to renal hemorrhage; in the brain, with resulting paralysis or softening; in the intestines, with bloody stools. The retina, conjunctiva, gums, parotid gland, and stomach may be affected. In some cases there is acute jaundice, with symptoms simulating acute yellow atrophy of the liver, and, as just stated, these lesions are not

merely mechanical, but infectious, and apt to give rise to suppuration.

When acute endocarditis is due to recurrence of inflammation in a valve previously fibrotic, abscesses are unusual.

The duration of the disease in the milder cases is usually from two to six weeks, perhaps in most instances about four weeks. The malignant cases may reach a fatal termination in one or two days, or, again, they may be prolonged for several months or a year, and then prove fatal. Some cases of simple endocarditis are not suspected during their course nor betrayed by sequelæ; thus, minute vegetations may be found, *post mortem*, upon the valves of patients who die of consumption or of carcinoma, which have been of no importance whatever. The great harm that simple endocarditis does the patient is not immediate, but consists in laying a foundation for ultimate changes in the valves, which impair the functional integrity of the heart.

As seen in practice, infective or ulcerative endocarditis does not always correspond with the description in books. In a series of cases witnessed by the writer, the most prominent symptom was oscillation of the temperature, with rigor or evidence of infarction. Other symptoms were petechiæ of the extremities, vomiting, ashy discoloration of the skin, and heart murmurs. N. Tirard (Practitioner, Nov., 1908).

*Nervous symptoms* which may be present and of some diagnostic service in prolonged malignant endocarditis have been emphasized by the writers. Sometimes nervous symptoms may dominate the clinical picture, as in a fatal case the writers report, in which Kernig's sign, neck rigidity, aphasia, flaccid hemiplegia, facial paralysis, and Babinski's sign were present. Occasionally these symptoms occur early

instead of late. In general, they are atypical and diffuse. The meningeal signs may be due to circumscribed hemorrhages. The condition may suggest tuberculous, cerebrospinal, or syphilitic meningitis, or acute tuberculosis. Lumbar puncture and blood cultures are important aids in the diagnosis. Claude and Oury (Rev. de méd., Aug.-Sept., 1922).

**DIAGNOSIS.**—The first question to settle with regard to diagnosis is whether any endocarditis exists at all, and, secondly, whether the form is simple or malignant. There may be no objective cardiac signs distinctive of the disease. Usually, however, there is a systolic apical murmur, and the heart is enlarged, with a more widely diffused impulse than normal, and an excited—though feeble—action.

It should be borne in mind that many of the diseases with which acute endocarditis is etiologically associated give rise to functional cardiac murmurs, so that the mere discovery of an abnormal sound over the heart does not establish the diagnosis.

**Typhoid fever** is more gradual in its onset and has a small number of white blood-corpuscles contrasted with the leucocytosis of endocarditis, and an infrequent pulse. Moreover, the Widal reaction is distinctive of typhoid, as would also be the discovery of typhoid bacilli in the blood or the stools. Typhoid may give rise to infarctions, and to inflammation of the parotid, but not often.

**Acute tuberculosis** has its hectic fever, rapid wasting, possible pulmonary signs, sometimes tubercle bacilli, and, as a rule, no objective cardiac symptoms.

**Malarial fever** may be recognized

by the discovery of the characteristic organisms in the blood.

**Septicemia** and **pyemia** have symptoms identical with those seen in certain forms of malignant endocarditis, which disease has, indeed, been called an arterial pyemia. In some acute cases there is possibility of confusion with typhus fever, cerebrospinal meningitis, abscess of the liver, and hemorrhagic small-pox.

In **severe infectious diseases**, unless there be signs of obstruction of a valve, it may be impossible to determine whether there be endocarditis or a myocarditis due to toxins, rendering the wall flabby and the mitral valve relatively incompetent.

Painful nodules in the skin, petechiæ in the skin, mouth and conjunctiva; Gram-positive diplococci in the urine when a local cause can be excluded; and the characteristic diplostreptococcus in the blood are all suggestive signs. Dickson and Wilbur (Calif. State Jour. of Med., Nov., 1914).

The writer bases the diagnosis of septic endocarditis in many cases on findings other than positive blood-cultures, viz., (1) Irregular fever for many months. (2) Absence of demonstrable lesions other than those of the heart. (3) Minute petechiæ. (4) Development of loud, harsh murmurs. (5) Marked irritability of the heart, shown by overaction, and wide fluctuations in the pulse-rate and character, irrespective of the temperature-curve. Pyorrhea alveolaris may account for many otherwise obscure cases. W. Gilman Thompson (Vt. Med. Mthly., Feb., 1914).

The writer found the *spleen* often greatly enlarged in patients who had died of acute or recurring endocarditis, independently of liver enlargement. It also occurred in cases of non-cardiac streptococcic infection, and about half as often in chronic cardiac disease. He considers it an important diagnostic sign in acute and recurring endo-

carditis. J. H. Arnett (Amer. Jour. Med. Sci., Apr., 1922).

**ETIOLOGY.**—Endocarditis is an infectious disease, and almost always secondary to some other. It is most frequently an expression of rheumatism. It may follow tonsillitis, pleurisy, chorea, measles, small-pox, and any acute infectious disease, particularly scarlet fever. Pneumonia, influenza, erysipelas, gonorrhea, pericarditis, and meningitis may present this complication, as may also, in rare instances, typhoid fever, tuberculosis, and diphtheria.

The writers compared 80 cases of *subacute bacterial endocarditis* that came to necropsy with 35 cases of rheumatic endocarditis, 18 of which also came to necropsy. The remaining 17 were typical cases of rheumatic endocarditis clinically. *Streptococcus viridans* was isolated from all of them. Rheumatic lesions can be produced in rabbits by injecting streptococci. Those of the viridans strains seem responsible for rheumatic and subacute bacterial endocarditis. Clawson and Bell (Arch. of Int. Med., Jan. 15, 1926).

Osteomyelitis, puerperal fever (as well as other vaginal or uterine affections), empyema, bronchiectasis, external wounds, and any form of septicemia may occasion endocarditis. Cancer, gout, diabetes, and Bright's disease may also give rise to this disorder.

Almost invariably some form of bacteria is found in the lesions, but there does not seem to be any bacterium peculiar to the disease. In rheumatic cases Small incriminates the *Streptococcus cardioarthritidis*, but in both the simple and malignant forms the ordinary pyogenic micro-organisms are those most often encountered, namely, streptococci, staphylococci, pneumococci, and gonococci.

Case of *meningococcus endocarditis* with septicemia. The meningococcus, in spite of its affinity for the meninges, may at times become lodged on the endocardium, with the production of an acute vegetative endocarditis. In this respect it resembles most of the other pathogenic bacteria, which, while showing a predilection for some particular organ or tissue, may occasionally produce serious lesions in other parts of the body. The symptoms and pathological anatomy of meningococcus endocarditis correspond to those which characterize malignant endocarditis of streptococcus or pneumococcus origin. It may or may not be associated with cerebrospinal meningitis. Cecil and Soper (Arch. of Intern. Med., July, 1911).

Diseases of the heart should not be regarded from the old standpoint of stenosis or regurgitation of a certain valve, but the heart should be treated as an organ invaded in the process of a bacteremia. From this point of view a careful etiological qualification of the infective agent should be studied. The symptom-complex arousing suspicion of acute endocarditis consists of the presence of an apical systolic murmur not modified by pressure with the stethoscope or by respiratory pauses, an irregular pulse, and a misplaced apex beat with or without an increase in cardiac dullness following any infectious process. Other symptoms may be embolism producing hemiplegia, and also punctate hemorrhages into the skin and mucous membranes, while a blood culture and leucocyte count may aid in diagnosis. G. H. Withers (Ill. Med. Jour., Apr., 1917).

Two cases of endocarditis occurred in young girls, sisters, and the only 2 children in the family. Both had attacks of tonsillitis, chorea, rheumatism and resulting cardiac trouble as a sequel. Both patients had 2 attacks of acute endocardial inflammation, followed by cardiac decompensation, with kidney breakdown. Both girls had not begun to menstruate, although 14½ years of age. The attacks came

on at the same age. The older girl died several years ago, and the younger one has just gone through a severe second attack of acute endocarditis and is now suffering from a marked enlargement of the heart, cardiac decompensation and parenchymatous nephritis with general anasarca. H. I. Goldstein (N. J. Med. Soc. Jour., Jan., 1918).

A state of *subacute bacterial endocarditis* of the *Streptococcus viridans* type was observed in 17 patients by the writer. In any heart case with irregular, remittent fever, loss of weight, joint pains, myalgia, progressive anemia of secondary type, anorexia, moderate leukocytosis, and the characteristics of a mild or moderate septicemia, persistent blood cultures should be made, and the organism will be found in 90 per cent. The majority of the author's cases began with a throat infection. L. H. Behrens (Ann. of Clin. Med., Sept., 1924).

Before birth the right side of the heart is almost exclusively affected; after birth, the left. Early adult life furnishes a majority of the cases, and, according to some late statistics, men are somewhat more liable to the disease than women.

Several cases have been ascribed to traumatism.

Case of a musician, aged 35, who, returning from a playing engagement in the early morning hours, was attacked by foot-pads. He escaped and reached home utterly spent and exhausted. For half an hour he had to stand up and struggle for breath. The sense of suffocation, however, gradually left him and was followed by a depressing palpitation lasting until the next day. Two or three months later it returned and has been intermittently troubling him ever since. Examination showed a presystolic thrill in the apex region, a loud churning presystolic mitral murmur, accentuation of the second pulmonic sound and also, on a later examination, a doubling of the second sound at the base of the heart. Before

the episode mentioned he was perfectly sound and well so far as known and his history was negative as regards disease. While admitting the difficulty of proving a given case of heart disease to be the result of trauma, the writer believes the endocardial lesion was the direct result of the violent strain and exertion. D. Riesman (Jour. Amer. Med. Assoc., Sept. 30, 1911).

**PATHOLOGY.**—It has already been said that clinically there is no dividing line between the simple and malignant forms of endocarditis. This is also true pathologically. The simplest lesions consist of minute warty vegetations, varying from 1 to 4 mm. in diameter, seated upon the valves. These are composed of fibrin, leucocytes, blood-platelets, and micro-organisms. Sometimes the vegetations are so abundant as to obstruct the valvular orifice. Even in the simple form (endocarditis verrucosa) there is more or less ulceration of the valvular endocardium. In the malignant form (endocarditis ulcerosa vel diphtheritica) necrosis is more extensive. The valve may be so thinned as to give way under the pressure of the blood, thus producing a valvular aneurism, or actual perforation of the valve. A portion of the valve may be broken off, or some of the chordæ tendinæ may be ruptured.

Case in which rupture of the chordæ tendinæ followed an attack of acute endocarditis during which the chordæ became enlarged and softened, pathological changes which favored their rupture. Fifty cases of ruptured chordæ were found in literature, divided into 5 classes. In 7 cases the rupture was due to severe traumata, such as fractured ribs from violent compression, falls from a considerable height, stab wounds, gunshot wounds, and the kick of a horse. Five cases were due to efforts, such as straining, lifting, excessive fatigue, and severe cough in which

no endocardial lesions were disclosed by the autopsy. In 9 cases the rupture was due to or preceded by strain, without endocardial or myocardial lesions. In 19 cases, in which no endocardial lesion was found, there was no history of strain or trauma. The writer's case had a presystolic murmur without mitral stenosis. L. F. Frissell (Med. Record, April 20, 1912).

The vegetations are situated mainly on that surface of the valve which is opposed to the blood-current. Thus, the lower surface of the aortic valves and the upper surface of the mitral valves are chiefly affected.

As the result of a study of 287 cases of endocarditis, both acute and chronic, which came to the autopsy table, the author found that myocardial disease is present in greater or less degree in practically all cases. In most instances the myocardial change is not determined by and is not the direct result of the endocarditis, but is caused independently by the same, affiliated, or entirely independent conditions. The form most frequently seen in chronic or late acute cases is fatty degeneration, a lesion which differs in no material histochemical respect from that involving voluntary muscle. From analogy, it seems that this degeneration in most instances succeeds a primary parenchymatous alteration. As a sequence to fatty degeneration, fibrous replacement and probably brown atrophy frequently appear. Treatment in endocarditis is mostly based on recognition of the dominance of the muscle factor, and in nearly all, except possibly syphilitic, cases it is without effect on the valvular change. Harlow Brooks (Amer. Jour. Med. Sci., Dec., 1911).

To ascertain how an infection takes place, whether by direct inoculation or by septic emboli and thrombi in the vessels of the leaflets the writer conducted an investigation. His results agreed with those of Ribbert, Orth and others, that the cocci were deposited upon the leaflets from the circulating blood and not within them as emboli. The possibility of an embolic origin of

endocarditis in man is not denied, yet none of the experiments furnishes any basis for such a belief. Lissauer (Zentralbl. f. allg. Path. u. path. Anat., March 15, 1912).

Exceptionally the heart wall suffers, sometimes leading to cardiac aneurism, or perforation of the ventricular septum, or perforation into the pericardium.

The associated lesions peculiar to endocarditis are mainly caused by emboli, and, yet, it is a surprising fact that sometimes, even when the valvular lesions are decidedly ulcerative, no evidence of embolism may be found *post mortem*.

The term "*endocarditis lenta*" is applied by the writer to an infection localized in the endocardium, the germs sallying forth thence occasionally into the blood. The germ in question he had isolated ten years ago, entitling it the *Streptococcus mitior seu viridans*; it is not very virulent but induces necrosis in parts of the endocardium, leading to wart-like efflorescences and causing a clinical picture distinguished by the insidious onset, the vague slight pains in the joints and groups of muscles, with palpitations and dyspnea and a dry cough, the latter causing the suspicion of a lung rather than of a valvular affection, especially if the patients are pale and anemic. In the cases in his experience there were evidences of mitral endocarditis. At first there were no audible murmurs in some cases, but the persistent fever suggested the true diagnosis. Schottmüller (Münch. med. Woch., March 29, 1910).

Schottmüller's *endocarditis lenta*, caused by the *S. viridans*, has a sufficiently distinctive picture to deserve recognition as a separate clinical entity. While cases of chronic endocarditis may also be due to the *B. influenza*, *S. pyogenes*, or pneumococcus, such cases should be distinguished from those due to *S. viridans*, just as epidemic cerebrospinal meningitis, for example, is distinguished from meningitis due to the

*B. tuberculosis*, *B. influenza* or *S. pyogenes*. Major (Bull. Johns Hopkins Hosp., Nov., 1912).

Anhemolytic streptococci were isolated in 9 out of 11 cases by the writer. One case recovered following large doses of sodium cacodylate intravenously. W. L. Bierring (Wis. Med. Jour., Nov., 1923).

Embolism affects the spleen and kidneys most frequently, and also many other organs, as above enumerated. If the right side of the heart is affected, there may be multiple pulmonary abscesses.

A study of the lesions produced experimentally by the injection of sparteine sulphate followed by the injection of adrenalin chloride showed that drugs introduced into the circulation produce proliferative changes in the endocardium. The most marked changes were in the endocardium covering the papillary muscles, though they occurred elsewhere, even in the auricles. The valves were free in most cases. The endocardial lesions were practically confined to the animals that received sparteine sulphate and adrenalin chloride. Uranium nitrate, potassium bichromate, and arsenic in various forms caused constant renal changes, but had no effect upon the endocardium. Christian and Walker (Proc. Amer. Soc. Adv. of Clin., 1910).

**PROGNOSIS.**—First, it is possible for very slightly developed cases of simple acute endocarditis to recover without any real damage. The great danger from the non-ulcerative form, besides embolism, is the setting up of a chronic fibroid deterioration of the valve, ultimately impairing its efficiency.

In rheumatic endocarditis the presence of rheumatic nodules over the bony prominences of the joints, in children and young adults, indicates that the attack is severe.

The malignant forms are almost invariably fatal. Cases in which the

acute process has been kindled upon the remains of a former valvular inflammation are somewhat more hopeful.

**TREATMENT.**—First, **prophylaxis**: Persons with rheumatic tendencies should be guarded against attacks by **cold sponging, woolen underclothing, and avoidance of cold and wet.** The tonsils, being a frequent gate of entrance for rheumatic and other infections, should be put in good order.

When in a case of acute endocarditis examination shows any morbid condition of the tonsils, pure **tincture of iodine** should be applied to them with a camel's hair pencil, daily. EDITORS.

Rheumatism and endocarditis are in great measure results of diseased or **infected tonsils** which should be **removed.** Even as a prophylactic measure such tonsils are better out than in. B. R. Shurly (Detroit Med. Jour., Feb., 1911).

In a study of the sequelæ of acute tonsillitis the writer refers to 6 cases in which **tonsillectomy** was performed during an attack of acute endocarditis with distinct benefit as regards the cardiac disorder. The milder attacks of tonsillitis are more apt to be followed by arthritis than the severe. Cultures should be made from the tonsil in all cases of joint or heart involvement and properly preserved. Harrison (So. Med. Jour., viii, 59, 1915).

In *endocarditis* complicating acute infections, resort should be had to surgical measures for the **removal of foci of infection** during the cardiac inflammation. C. A. Ray (South. Med. Jour., Oct., 1924).

Patients who simultaneously suffer from rheumatism should be kept as quiet as possible. The salicylates do not seem to lessen the liability of such patients to endocarditis. It may be that the administration of **alkalies** in

sufficient amounts to keep the urine neutral is of some advantage.

The use of **salicylates** and alkalies for the suppression of the rheumatic poisons is the best means by which the effects of that poison on the cardiac tissue can be overcome. The application of **leeches** or of **ice** or of a succession of **small blisters** or of **iodine** over the **precordium** are all measures of relief useful in many instances. Choice must be made of the one most suitable to the requirements of the case on hand. In many instances the pain and restlessness in the earlier stages of the illness are so intense as to necessitate the use of **morphine.** On the first evidence of cardiac failure **strychnine** ought to be given hypodermically and should be combined with **digitalin,** should the pulse, despite strychnine, remain small, quick, and irregular. If dyspnea becomes urgent, and especially when it is accompanied by cyanosis, recourse should be had to inhalations of **oxygen.** Rankin (Practitioner, July, 1911).

In the various children's diseases the only way in which we can protect the patients from cardiac complications is by insuring **bodily quiet** and good ventilation and avoiding exposure to cold.

In gonorrhea such internal antiseptics as **salol** and **urotropin** are advisable.

Second, when the disease has actually developed, an **ice-bag** wrapped in flannel may be kept over the heart if not disagreeable or depressing to the patient. Or, instead of this, a thin **layer of cotton-wool** may be applied. Violent counterirritants are not indicated.

If the action of the heart is excited, **bromide of sodium** may be administered. Still more efficient, and in case of cardiac distress indispensable, is **morphine,** used in carefully regulated

amounts. In septicopyemic affection, besides the local measures, good results with 0.3 or 0.5 Gm. (5 to 7½ grains) **quinine hydrochlorate** several times a day to act on the bacteria in the blood are obtained.

If there is stagnation of pulmonary circulation, **ammonium carbonate** is indicated. **Aromatic spirit of ammonia** is a good stimulant. If rheumatism is connected with it, **chloride of gold**, ⅛ to ¼ grain (0.008 to 0.016 Gm.) three times a day, is a fine remedy in this condition; so is fld. extr. **cimicifuga**, 15 to 20 drops three or four times a day. Its antispasmodic, diuretic, and diaphoretic action is valuable and efficient; small doses increase secretion; full doses increase the force of the heart and slow the rate. **Cimicifuga** is a valuable remedy in endocarditis and other heart trouble. **Ammonia** is a good stimulant, but **whisky**, or **brandy**, is the best general stimulant we have. **Sparteine sulphate**, ⅛ to ¼ grain (0.08 to 0.016 Gm.) is a good stimulant and tonic. These two last, used hypodermically, slow and strengthen the heart beat and increase the cutaneous and venous circulation. The author has used **adonis vernalis** successfully in combating "heart-failure," pain, and dyspnea—tincture, 10 drops; **adonidin**, ⅓ to ¼ grain (0.016 Gm.) every three or four hours. E. C. Rothrock (Wisc. Med. Recorder, June, 1908).

Where there is marked danger of heart paralysis from acute dilatation nothing seems to be better than **strophanthin**, in doses of ½ to 1 milligram (⅓<sub>20</sub> to ⅓<sub>65</sub> grain) given directly into a vein. The action is very rapid, but unfortunately does not persist very long; so that it must be repeated, or other remedies must also be given. The drug is not so dangerous as some authors would have it, and as much as 1½ milligrams (⅓<sub>40</sub> grain) daily have been given on two successive days, and 8.5 milligrams (⅓<sub>6</sub> grain) altogether in eight days. The cumulative action is very slight. Within a few minutes the pulse will fall in frequency, will become more forcible, and the dyspnea and

cyanosis will disappear. The drug is generally regarded the last resort in cases of extreme cardiac weakness, though it may fail when **camphor** will still revive the heart. Where a more lasting action is desired, subcutaneous doses of **digitalone** or **digitalin-Nativelle** are in place. The latter resembles **strophanthin** very closely, but acts more slowly, while the action of the former is more prolonged. The technique of intravenous injection is very simple. It is better, however, first to introduce the needle without the syringe into the vein, so that none of the **strophanthin** solution will be deposited into the subcutaneous tissue. O. Hornung (Münch. med. Woch., Sept. 26, 1908).

Of great importance in these cases is **absolute bodily quiet**, and this should be maintained for at least four to six weeks. In case the heart begins to fail, recourse must be had to **digitalis**, **strophanthus**, **alcohol**, **ammonia**, and other cardiac stimulants, but in many cases their use will prove unavailing. Sometimes when the attack has been long continued, **arsenic** has been found beneficial.

In 2 cases of malignant endocarditis treated by the writer in which blood cultures showed the presence of *strep-tococcus viridans*, an organism which produces a subacute but extremely fatal form, he obtained recovery in one case by injecting intravenously **salvarsan**. He has tried a great variety of other methods of treatment in such cases without success. Lorey (Münch. med. Woch., April 30, 1912).

James Mackenzie is inclined to believe that in rheumatic endocarditis the **salicylates** may do good. He says that their employment is so frequently of use that it should always be tried, even pushing it at times. Lee states that large amounts of **salicylate of sodium** may be safely given, provided the bowels are kept open and the urine is kept alkaline with



**bicarbonate of sodium**, and provided, also, that the salicylate is temporarily suspended if unpleasant symptoms are produced.

To promote sufficient refreshing sleep, moderate doses of **bromide** may be found useful, but if not, other drugs should be used. The writer prefers among the various hypnotics **chloral-amide** or **trional**, but if these do not suffice, **chloral** or **morphine**. The former is reliable, but its depressant effects must be considered, and he would give it only in the excited sthenic heart of rheumatic endocarditis; in the myocardial involvement, especially of pneumonia and diphtheria, he would not employ it. Morphine is reliable and safer. F. S. Meara (Jour. Amer. Med. Assoc., Feb. 3, 1912).

In streptococcic endocarditis, **anti-streptococcic serum** occasionally succeeds. In all cases of septic endocarditis, diagnosed early by blood examination, **antistreptococcic serum** should at first be tried. If this fails, intravenous **arsphenamin** should be considered, and as a last resort, **splenectomy**. E. Munzer (Zentr. f. inn. Med., Apr. 17, 1920).

Case in which acute endocarditis had followed sore throat. A streptococcus having been isolated from the blood, another person was immunized with a vaccine made from it and 4 **blood transfusions** of 500 to 600 c.c. each were carried out from this person to the patient within 5 weeks. A favorable effect on the blood was noticed and the patient's strength was maintained by the procedure to a marked degree, but there was no definite change in the temperature, and death ultimately occurred. Levison (Jour. Lab. and Clin. Med., Jan., 1917).

The writer carried out a procedure similar to the above in a case of malignant *S. viridans* endocarditis, a definite temporary improvement resulting. G. F. Dick (Jour. Amer. Med. Assoc., Apr. 22, 1922).

Case of subacute infectious endocarditis, confirmed by blood culture, in which series of daily injections of an

**autogenous vaccine** seemed to benefit, the patient living nearly 2 years. Fontanel, Devic and P. Durand (Lyon méd., Jan. 20, 1924).

Report of a case of joint pains and severe endocarditis in which 3 **immunotransfusions** were followed by marked improvement, the patient returning to his work. E. Wordley (Lancet, Aug. 2, 1924).

Prompt response to injections of **gentian violet** in a case of subacute infective endocarditis. Hofer had found malachite green and crystal violet in experimental guinea-pig septicemia markedly bactericidal. Major (Jour. Amer. Med. Assoc., Jan. 24, 1925).

**Specific sera and vaccines** have also been used, but are not very promising.

Various antistreptococcal serums, especially the so-called polyvalent variety, have been tried, but in view of the various micro-organisms, not to mention the many strains of streptococci, which may be responsible for the disease, it is rather hard to select the proper serum. The **vaccine** treatment would seem to afford a better chance of success, but when one considers how difficult it must be for the protective substances, even if formed, to reach the micro-organisms deeply seated in the affected valve through the very imperfect and slender channels through which the blood-supply reaches the valve, the chances of success do not seem very promising, and the vaccine treatment will in no way lessen the dangers of embolism. Moreover, in acute generalized infections, the vaccine treatment is not so helpful as in the case of focal lesions. Broadbent (Practitioner, July, 1910).

### CHRONIC ENDOCARDITIS.

Chronic endocarditis may develop in a previously healthy valve. It is more often a sequela to acute endocarditis.

**SYMPTOMS.**—The symptoms are those of valvular disease of the heart, and are discussed under the next general head.

In the diagnosis of chronic endocarditis, it is important to adopt routine in the examination of the case in order not to overlook the condition present. The following order was adopted: Mitral incompetency, mitral stenosis and aortic regurgitation. True organic mitral regurgitation conforms to the following picture: 1, Soft, blowing, systolic murmur, best heard at apex, but transmitted to axilla and to angle of left scapula; 2, accentuated pulmonic second sound; 3, enlargement of the heart—apex displaced downward and to the left, so that inspection and auscultation afford the greatest information in this condition. In mitral stenosis the chief clinical findings are (1) a presystolic thrill, rough, grating, felt in fourth or fifth interspace inside nipple line, ending in (2) a sudden, snappy shock, synchronous with ventricular systole; (3) a rough, presystolic murmur heard in and usually limited to the area of thrill, ending in (4) a loud, snappy first sound at the apex; (5) accentuation of second sound in pulmonary area. Aortic incompetency presents the following group of signs: 1, The greatly displaced apex beat; 2, a long-drawn diastolic murmur heard at the base of the heart and best in the aortic area; 3, pulsating vessels in the neck, and 4, the water-hammer pulse of Corrigan. Rowntree (*Jour. Med. Soc. of N. J.*, Feb., 1908).

In a series of 14 cases the disease manifested itself clinically over varying periods of time. In one patient, the symptoms began two years before the real condition was recognized. One case began fourteen months before a definite diagnosis was made. Another patient probably suffered from the disease for more than two years, and in the earlier part of the illness the diagnosis of typhoid was made for a condition which was, in all probability, infectious endocarditis, the diagnosis having been based on the fact that there was fever and splenic enlargement. No rose spots were found; there was no diarrhea, and the Widal reaction was negative throughout.

The infectious organisms found in

the writer's 14 cases were as follows: The pneumococcus, 11 cases; streptococcus, 3 cases. The organisms obtained in the 11 patients suffering from pneumococcemia had many of the morphologic characteristics of streptococci. Study of the organisms in culture and in animals proved that they were the pneumococcus. In one patient of this series the infectious endocarditis followed pneumonia. Tonsillitis had occurred in 2 cases. In the other patients the source of infection could not be learned. There can be no doubt whatever that simple local infection like tonsillitis, as well as abscess of the aural cavities, infection of the postnasal space or the antra, and so forth, may be the port of entry. In some cases of this series the infection was implanted on an old endocardial or valvular scar. F. Billings (*Arch. of Intern. Med.*, Nov., 1909).

Of the 76 patients with chronic and recurring verrucous endocarditis at the Basel university medical clinic, during the last four years, 16, that is, 21 per cent., recovered without any consecutive clinical functional disturbances. Even in cases in which a serious valvular defect was known to exist, the functional outcome was remarkably favorable. C. Amsler (*Correspondenzbl. f. schweizer Aerzte*, April 10, 1912).

Patients with chronic septicemic endocarditis and splenomegaly may become bacteria free and yet succumb. The spleen is always enlarged and obscures the underlying heart effect. The disease may be mistaken for splenic anemia. The accumulation of bacteria in the spleen often prevents cure of the disease. In the case of a man 57 years of age, in whom Deaver removed the spleen, the condition cleared up after operation. Riesman (*Trans. Assoc. Amer. Phys.*; *N. Y. Med. Jour.*, Sept. 14, 1918).

The basal metabolic rate was found considerably increased in some cases of endocarditis lenta, in spite of the days or even weeks of normal temperature interrupting the usually slightly febrile course. H. Gessler (*Arch. f. klin. Med.*, June, 1924).

The presence of bacteria in blood cultures of patients with endocarditis is generally regarded as indicating a grave prognosis. This idea is not altogether in harmony with results obtained at St. Luke's Hospital, Chicago. Of 57 patients with bacterial endocarditis, 24 are living and many of them seem to have recovered from the heart valve infection. The other 33 are dead. Biggs (Arch. Internal Med., Mar. 15, 1925).

The application of pressure around the arm produces minute petechial hemorrhages below the area of the compression in patients with scarlet fever. This *Rumpel-Leede phenomenon* is never observed in normal persons with the exception of women during the menstrual period. It is caused by pathologic changes in the capillary endothelium. The writer found it to be positive in most patients with endocarditis lenta and with essential hypertension. Weissmann (Zeit. f. klin. Med., Aug. 20, 1925).

### ETIOLOGY AND PATHOLOGY.

—Besides being a possible sequela of acute endocarditis, the chronic form may be produced through the influence of certain predisposing causes, namely: Gout, alcohol, syphilis, and habitual muscular overexertion, particularly if in the individual there is a tendency to arteriosclerosis. Exceptionally, the wall of the heart itself is affected by the process, in which case it presents scar-like patches, which are often associated with myocarditis. There is also a form of chronic pneumococcic origin.

The organism of chronic pneumococcus endocarditis should be considered as a modified pneumococcus in that it produces an endocarditis by first causing an embolic hemorrhage which serves, in turn, as a culture medium for the organism. Growth begins, then, before the leucocytes gain entrance to destroy the bacterial clump. A vegetation is the result. The writer holds that

the form of endocarditis known clinically as subacute or chronic infectious is due, in the vast majority of cases, to organisms of practically no virulence in the ordinary sense. Death is due to exhaustion, the result of prolonged parenteral protein intoxication. Rosenow (N. Y. State Jour. of Med., Aug., 1912).

Other germs besides streptococci may cause the affection which had been described clinically by other authors before it was called by Schottmüller "endocarditis lenta." The *Streptococcus viridans* seems to be a form changed by the infected organism—instead of being the specific agent. The leukocyte count varies not only in different stages of the disease but also according to the place (ear, finger, vein) where the blood was taken. Endothelial cells may be found almost constantly in the first drop dripping from the ear. Hemorrhagic nephritis is almost constant, and predominates clinically in a number of cases. Red cells are always found in the sediment—sometimes with only a slight or negative reaction for albumen. The Wassermann reaction is frequently positive (in 15 out of the 77 cases). Emboli and infarcts are common. The disease may clinically begin and end with an embolus or an aneurysm. One patient recovered, although the nephritis persisted. F. O. Hess (Münch. med. Woch., Feb. 6, 1925).

Valves changed by chronic endocarditis are more or less opaque, thickened, and cicatricial or calcified. They may be contracted, deformed, curled up, and adherent by their edges to one another.

The chordæ tendinæ may likewise be involved in the morbid process and thereby be deformed, or fastened one to another, or greatly contracted so that the distorted valve is apposed to the muscular papillæ. The apices of the papillæ themselves may be more or less fibrotic. Fetal endocarditis is usually of this chronic form.

## LEADING SIGNS OF ORGANIC HEART DISEASE. (SAJOURS.)

(See location of sounds in the opposite plate.)

**MITRAL DISEASE.** Most frequent of all.

**Auscultation Center:** fifth left interspace below apex, blue spot No. 1. Signs:—

### Regurgitation.

1st sound *Ffoo*; radiates toward axilla and back.

2d sound *Dub*; obscured.

Heart is enlarged transversely. Apex blow displaced downward and more diffuse. Area of percussion dullness enlarged. Pulse small and irregular. Pulmonary congestion and dyspnea. Edema, ascites, cyanosis, etc., appear late.

### Stenosis.

1st sound *Lub*; sharp and loud, or *Lub-Lub*.

2d sound *Ffroo*; harshly radiates toward axilla and back.

Presystolic murmur. Apex blow slightly to left of normal, and sharply localized. Pulse small, but regular, except in advanced cases. Percussion dullness increased to right. Pulmonary congestion and dyspnea. Edema, ascites, cyanosis, etc., occur late.

### Regurgitation and Stenosis.

1st sound *Ffoo*; radiating to axilla and back.

2d sound *Ffroo*, or *froo-lup*; short and combined.

Pulse small, rapid, and irregular, alternating, sometimes dicrotic. Percussion dullness increased. Pulmonary congestion, dyspnea, and cough. Edema, ascites, cyanosis, etc., occur late.

**AORTIC DISEASE.** Next in frequency to mitral.

**Auscultation Center:** second right costal interspace, blue spot No. 2. Signs:—

### Regurgitation.

1st sound *Lub*.

2d sound *Ffoo*; prolonged, sometimes double; may become harsh *Ffroo*; radiates upward into carotids and sometimes downward.

Pulsating arteries of neck characteristic. Systolic shock heard in brachial and other arteries. Corrigan or "water hammer" pulse; rapid, abrupt, and poorly sustained. Apex impulse forcible, heavy, and lowered to the left. Percussion dullness increased toward left.

Pallor characteristic; vertigo and sometimes syncope. Edema, ascites, hepatic congestion, etc., occur late.

### Stenosis.

1st sound *Fffoot*; prolonged whistling and harsh; radiates upward into carotids; sometimes downward.

2d sound *Dub*; weaker than normal.

No external pulsations. Displacement of heart; apex removed downward and to left. Pulse not heaving or bounding and less collapsible; sometimes hard. Palpitations.

### Regurgitation and Stenosis.

signs of both conditions may prevail.

1st sound murmur most marked and radiates into carotids.

Dyspnea, due to passive pulmonary congestion; cyanosis and dropsy occur early.

**TRICUSPID DISEASE.** Occasionally complicates mitral disease or dilatation.

**Auscultation Center:** lower end sternum, blue spot No. 3. Signs:—

### Regurgitation.

1st sound *Fee-oo*; radiates toward left nipple.

2d sound *Dub*.

Venous pulse in neck; pulsating, congested liver. Percussion dullness increased to right. No effect on pulse. Edema, ascites, etc., occur early.

### Stenosis.

Very rarely observed.

1st sound *Lub*.

2d sound *Ffroo*; harsh rolling; radiates toward left nipple.

Venous engorgement visible in neck without pulsation. Congested liver. Percussion dullness increased to right. Pulse small. Cyanosis, dyspnea, edema, ascites, etc., occur early.

**PULMONARY VALVE DISEASE.** The rarest of heart lesions.

**Auscultation Center:** second left costal interspace, blue spot No. 4. Signs:—

### Regurgitation.

1st sound *Lub*.

2d sound *Ffoo*; radiates upward to clavicle.

Inspiration sounds in lungs interrupted. Apex beat moved somewhat to left. Percussion dullness increased to right.

### Stenosis.

1st sound *Ffrrroo*; rough; radiates upward to clavicle, but widespread.

2d sound weak or absent or replaced by diastolic murmur.

Cyanosis an early sign; tendency to hemorrhages. Varicose dilatation of peripheral veins. Percussion dullness increased to right. Edema, ascites, etc., occur very early.

Occasionally met with in infants and tuberculous subjects.

### Regurgitation and Stenosis.

Extremely rare. Signs of both lesions combined.

## ENDOCARDITIS.

Signs according to the valvular structures involved; those of insufficiency or stenosis, as above, appearing in turn or together. At first soft, gradually become rough, sibilant, and grating. Signs recede as the case improves, unless chronic organic lesions engendered. Apex beat moved slightly to left. Percussion dullness slightly increased.

## PERICARDITIS.

**Before Effusion.** Friction murmur. Close to ear when patient sits up and therefore clearer; recedes when patient lies down. Coincides with heart sounds and does not radiate into vessels of neck. Presystolic murmur sometimes heard at apex. Percussion dullness normal. Yellow outline, No. 3.

**With Effusion.** Serum gradually fills pericardium; hence heart sounds, or murmurs, distant or lost and area of dullness increased, according to quantity of fluid present. Area finally becomes pyriform. Apex stroke against chest wall lost. Absorption of fluid indicated by return of murmurs beginning above and increasing as level of fluid descends, and clearing of heart sounds. Yellow outline, No. 6.

## MYOCARDITIS.

**Acute Form.** Heart sounds short, sharp, tumultuous, then become feeble. Valvular murmurs brought on by disease of heart muscle and sometimes by dilatation. Endocardial changes indicated by an increased pulmonary second sound.

**Chronic Form.** Impulse feeble and heaving. Apex stroke displaced downward and to left. Heart beats often greatly decreased in number and often intermittent. Attacks of angina pectoris and palpitations. Lesions of mitral valve frequently appear with gallop rhythm.

## HYPERTROPHY.

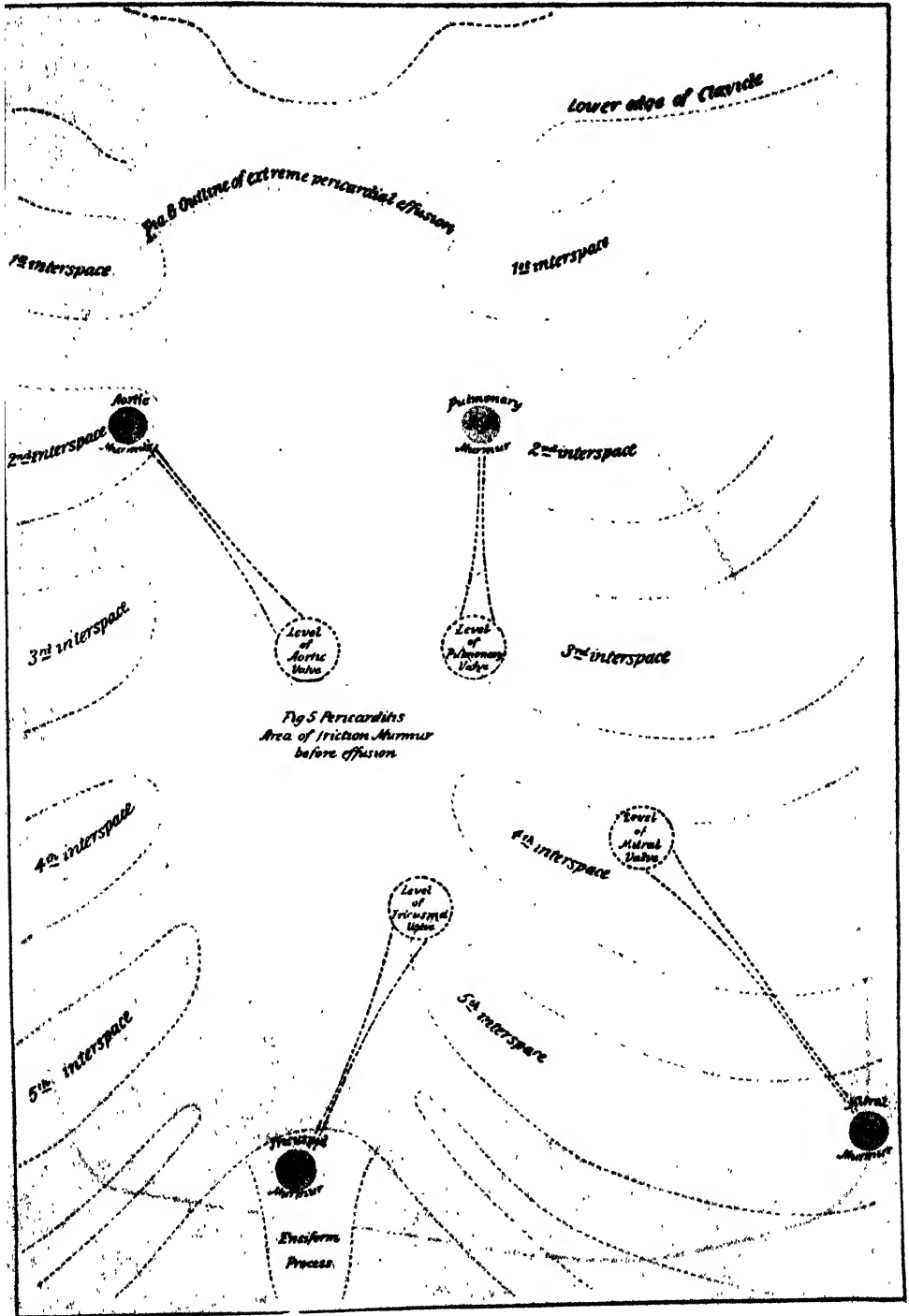
All heart sounds increased, especially aortic second sound. Irregular gallop rhythm in marked cases. Action heaving and vigorous. *booming*. Impulse at apex hard and diffuse. Murmurs indicate coexisting valvular lesions.

## DILATATION.

Signs of tricuspid insufficiency (see above). First sound short, sharp, and ringing. Venous pulsations in the neck and venous turgescence. Epigastric pulsation. Percussion dullness extended to the right. Pulse small, irregular, and rapid.

## FATTY HEART.

No characteristic sign except weakened heart action. When other signs appear they are those of dilatation (see above).



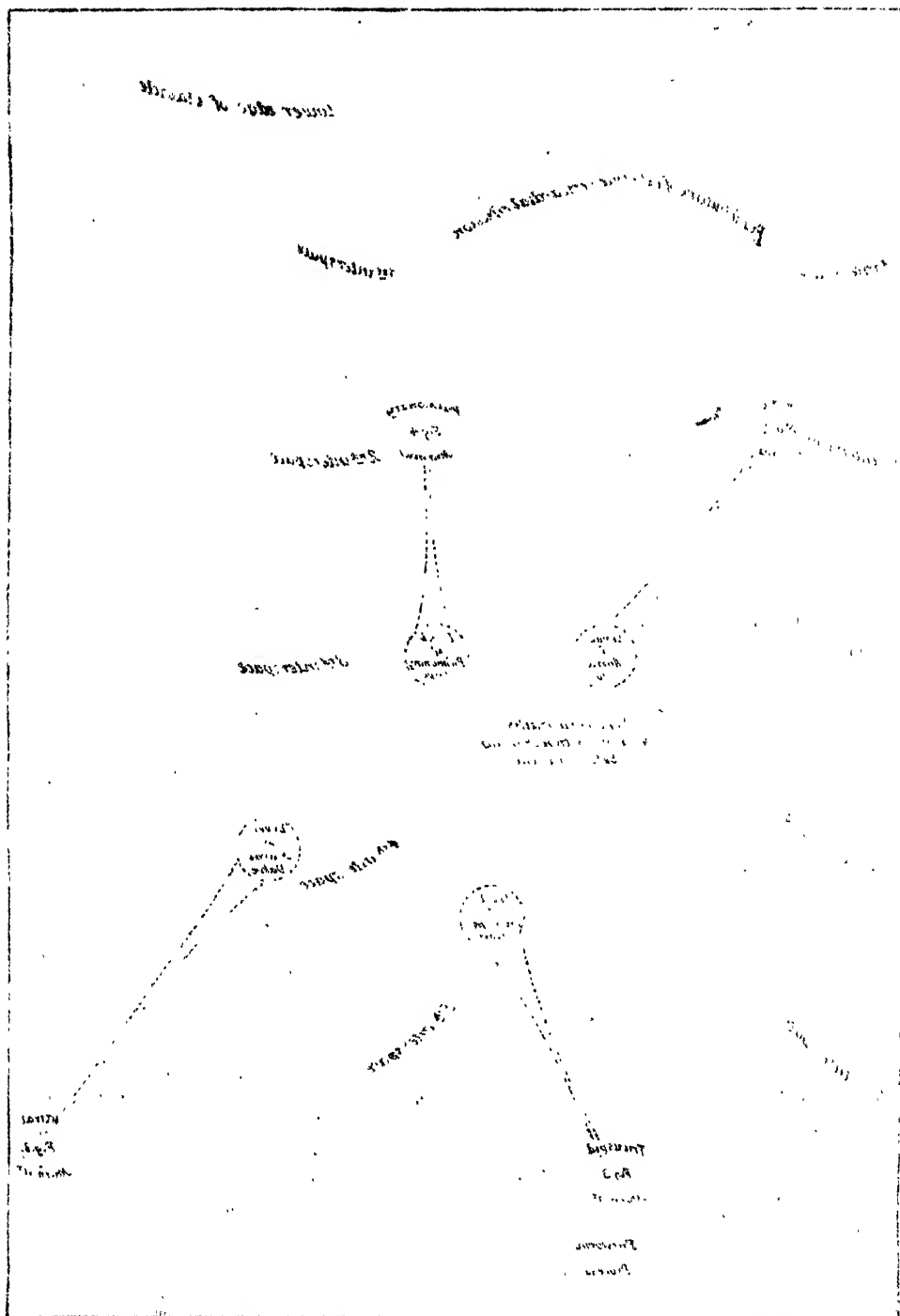
Section of Chest Over the Heart, Showing the Location of Cardiac and Pericardial Sounds. (Sajous.)

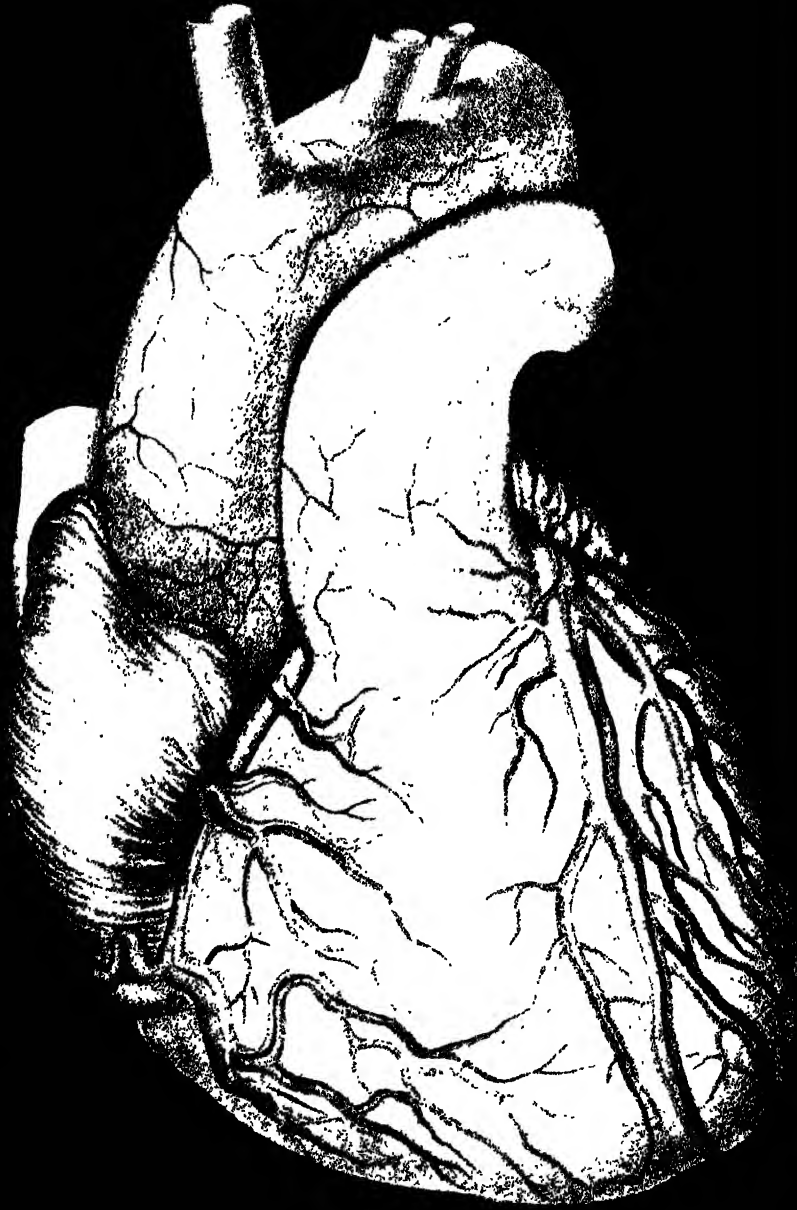
The blue spots indicate where the normal valvular sounds are detected stethoscopically. The yellow outlines indicate the relative area of extreme pericardial effusion.

concentrations of the relative size of extreme precipitation  
in the spot. Indicate where the normal rainfall amounts are detected meteorologically. The yellow

(1992) *Journal of Interpersonal Violence* 7, 1-10.

... showing the location of Cardiac









**TREATMENT.**—The treatment of chronic endocarditis being that of the valvular lesions, it will be described under the next general heading.

In the management of chronic endocarditis during the stage of compensation it is necessary, as emphasized by Stein, to individualize all cases, noting that every patient reacts differently to drugs, dosage, to different preparations, and to mechanical stimulation. All compensation is, of course, relative. Alcohol should be dispensed with, as also tobacco, tea, and coffee. All emunctories must be kept as nearly normal as possible. Rest in the recumbent position and sleep are all-important. In cases with insomnia, hydrotherapy is of great value as a hypnotic and cardiovascular regulator. If drugs are used, sodium and ammonium bromide are less depressing than the potassium salt, while the trional-barbital group are of great service. Codeine is, without doubt, the safest of the opium preparations.

In chronic infectious endocarditis, absolute rest, good air, sunshine, simple but nourishing food and tonics, but avoidance of drugging are indicated. Here, even autogenous vaccine or sera are more harmful than beneficial.

In a heart clinic strict rest in bed for weeks or months proved of great prophylactic value. Eustes (Boston Med. and Surg. Jour., Sept. 2, 1915).

After favorable experiences with sodium cacodylate in acute rheumatic pericarditis, it was used also in chronic infectious endocarditis with *Streptococcus viridans* bacteriemia. The daily dose should not exceed 0.6 or 0.7 Gm. (9¼ or 10¾ grains), subcutaneously or intravenously. Billings (Jour. Amer. Med. Assoc., July 1, 1922).

Distinct benefit from sodium cacodylate noted in rabbits inoculated

with *S. viridans* cultures from patients with infectious endocarditis. J. A. Bargen (Arch. of Int. Med., Nov., 1923).

In 8 cases of chronic infectious endocarditis with *S. viridans* blood cultures, the writer gave 1 to 4 grains (0.065 to 0.26 Gm.) of sodium cacodylate daily over a long period. Two patients died; 4 were well after intervals of 22 months to 11 years, and 2 were improved after 3 and 6 months. The drug was pushed until the breath had a strong garlic odor. The preparations on the market in ampoules not being very dependable, fresh preparation of a reliable drug every few days is advised. If the bowels became loose the dose was decreased for 2 or 3 days. Rest in bed was insisted on during the treatment. Capps (Amer. Jour. Med. Sci., Jan., 1923).

## VALVULAR DISEASES OF THE HEART.

See the annexed colored plate for the leading signs of the various valvular lesions.

**VALVULAR LESIONS.**—Whether or not the abnormal state of the affected valve causes incompetence or obstruction, there results in either case an unnatural demand upon the muscular power of the heart. Thus, stenosis leads to an increased effort during systole of that cavity which is obliged to force blood through the narrow outlet, and a leaking valve permits blood to flow backward into the cavity which it has just left, and thus obliges it to do part of its work a second time. In either case, the affected cavity is made to contain a larger amount of blood than normal.

In case either auriculoventricular valve leaks, the corresponding ventricle receives, during diastole, a larger amount of blood than normal from the overdistended auricle.

The heart possesses reserve forces,

and, while the immediate effect of a valvular lesion is dilatation of the chamber affected, the secondary result is hypertrophy of the muscular walls, and a more or less complete fulfillment of the new demands. Unfortunately, however, there is for several reasons a tendency to retrogression. In the first place, the valvular endocarditis may grow worse by slow change or because of a recurrent acute inflammation. Secondly, the myocardium is apt to deteriorate so that the muscular power of the heart diminishes. Thirdly, in some forms of valvular disease, particularly aortic, the coronary arteries from which the heart derives its nourishment are apt to be involved. The period during which the heart, having hypertrophied, remains equal to the demands made upon it is called the period of "compensation." Sudden exertion, great mental excitement, or the stress of intercurrent disease may cause a temporary "disturbance" of this compensation. Finally, extreme degrees of valvular deformity and myocardial degeneration bring about "ruptured compensation."

### MITRAL REGURGITATION.

**DEFINITION.** — Insufficiency of the mitral valves, permitting blood to leak into the left auricle during systole.

**SYMPTOMS.**—The subjective symptoms of mitral regurgitation depend upon the degree of compensation present in the individual case. Thus, if the condition is a favorable one, the patient may be unconscious of any unnatural state whatever, having no dyspnea except on considerable physical exertion. On the other hand, if the circulation is beginning to be em-

barrassed, we may observe palpitation, shortness of breath on exertion or excitement, cyanosis and, perhaps, edema of the dependent parts. On physical examination the heart is found to be enlarged mainly in its transverse diameter, the apex being pushed toward the left, and the limit of dullness extending farther toward the right than in health. The cardiac impulse may be more diffuse than in health, and visible in the epigastrium as well as in the normal position. In young subjects the precordia may be somewhat bulged. On palpation, a systolic thrill may sometimes be distinguished; this is not, by any means, the rule, however. On auscultation, we hear at the apex of the heart a murmur systolic in time and transmitted outward toward the axilla. This murmur is also audible inside the lower angle of the scapula. At the base the pulmonic second sound is accentuated and often reduplicated. The pulse in well-compensated cases may be nearly normal. In later stages it is rather small, frequent, of low tension, and irregular in force and rhythm.

The significant symptoms of failing compensation, dyspnea, cough, and hemoptysis sometimes appear before the physical signs. The gradual disappearance of a murmur and gradual weakening and final disappearance of the apex-beat have an evil significance. Carr (*Practitioner*, Sept., 1907).

Uncomplicated (primary) mitral insufficiency is one of the comparatively infrequent lesions, and should be diagnosed only if hypertrophy coexists. Butler (*Med. Rec.*, Sept. 18, 1920).

Where the chest is small and the auricle large, the murmur may be heard not only at the apex and axilla, but also over the auricle and, if the heart is in contact with the spine, also over the latter posteriorly, where it may even

be louder than anteriorly. Roch (Rev. méd. de la Suisse rom., Jan., 1923).

**DIAGNOSIS.**—The important factors in diagnosis are, first, the systolic murmur, which is usually heard loudest at the apex and transmitted outward, and which, in some instances, may be heard over a much more extensive area; in fact, almost all over the chest. Again, the murmur may be audible merely along the left edge of the sternum. The sound is of a blowing character, sometimes musical, especially toward its termination, and it replaces the first sound of the heart to a greater or less extent.

The second factor in diagnosis is the transverse enlargement of the heart. The apex may be lowered into the sixth space, but the main change is in the width of the cardiac dullness, which may extend from the left anterior axillary line to the right nipple.

Third, the pulmonic second sound, heard in the second left space or over the third left costal cartilage, is accented and perhaps reduplicated. Relative insufficiency of the mitral valve, with a normal condition of the valves, but with such dilatation of the left ventricle as to prevent the closure of the mitral orifice, may give rise to a precisely similar trio of signs.

It has been claimed that the only means of making the diagnosis of valvular incompetency as distinguished from relative insufficiency would be to find, in addition to the other signs, a presystolic murmur due to accompanying stenosis of the diseased valve. In many cases the history of the disease and the general appearance of the patient would be equally decisive. Functional or hemic murmurs may be heard during systole at the apex and transmitted outward, but they are not as-

sociated with enlargement of the heart or accentuation of the pulmonic second sound.

**ETIOLOGY.**—Deformities of the mitral valve leading to incompetency are caused by acute endocarditis, and still more frequently by chronic fibroid change. Relative incompetency of the mitral valves may be due to failing compensation in case of an aortic lesion; or to the terminal stage of idiopathic hypertrophy of the heart (meaning that condition of the myocardium which is seen after habitual excess in muscular exertion and in the use of alcohol); also to changes in the heart secondary to chronic nephritis, arteriosclerosis, and chronic adhesive pericarditis.

**PATHOLOGY.**—The diseased valves present characteristic changes. They are more or less opaque, thickened, and cicatricial or calcified, and as a result contracted, curled, or otherwise deformed. The edges of the valve segments and of the chordæ tendinæ to which they are attached are frequently more or less adherent one to another. In advanced stages the valvular orifice may be transformed into a rigid, calcified ring. The mechanical effects of mitral regurgitation are as follows:—

During systole blood escapes backward through the valve into the left auricle, which cavity, therefore, receives blood both from normal sources and from this new abnormal one. Consequently the left auricle becomes dilated, and, as a consequence of the new demands made upon it, hypertrophied, so that its walls may be three or four times the normal thickness. Moreover, the left ventricle receives with each diastole not only its normal quantity of blood, but an abnormally great amount from the dilated and hypertrophied left

auricle; so that it also becomes dilated and hypertrophied. As the valve lesions become aggravated, or the strength of the left auricle diminishes, the flow of blood from the pulmonary veins into the left auricle becomes impeded and the whole pulmonary circuit congested, thus putting a strain upon the right ventricle. It is the hypertrophied right ventricle which is the main factor in preserving a normal flow of blood in case of mitral regurgitation. At last the right ventricle fails,—dilates; the tricuspid valve becomes relatively incompetent; the right auricle is embarrassed, and finally the systemic circulation becomes congested.

Patients with mitral regurgitation before the advent of the subjective symptoms may be seen to be slightly cyanotic, and young subjects are apt to have clubbing of the ends of the fingers. As compensation fails, the lungs become congested and edematous and undergo brown atrophy; the liver, spleen, and kidneys present the lesions of passive congestion, the lower extremities begin to be edematous, and finally general dropsy and orthopnea appear.

**PROGNOSIS.**—Mitral regurgitation may exist for years without subjective discomfort, particularly if the patient escapes any great nervous or physical stress in life. Moreover, when compensation is impaired, judicious treatment will repeatedly restore the patient to a state of comfort. Finally, of course, the embarrassment cannot be alleviated and death ensues; but death is apt to be gradual rather than sudden.

Case of an infantry officer 25 years of age who came under observation for palpitation, shortness of breath, and depression as the result of gassing two months previously. He was

found to be in good physical condition, but examination of his heart revealed hypertrophy, marked aortic and mitral insufficiency, and probable aortic and mitral stenosis which evidently dated from an attack of rheumatic fever when he was 13 years old. His pulse was regular, moderate in rate, and of water hammer type. In spite of this severe cardiac valvular disease he had always been unusually athletic all of his life up to the time of his gassing, having been a leader in football, cricket, short distance running, broad jumping, and the champion athlete of his whole army corps. It is evident that in this case the heart had a greater reserve power, in spite of the valvular handicaps, than the average heart. R. D. Rudolf (*Brit. Med. Jour.*, Jan. 4, 1919).

**TREATMENT.**—With regard to treatment, much which is applicable to this subject will be given in the next volume, in the section upon DILATATION OF THE HEART, and other considerations will be discussed at the end of the section on VALVULAR DISEASES.

### MITRAL STENOSIS.

**DEFINITION.**—Mitral stenosis is a change in the mitral valves which impedes normal flow of blood from the left auricle into the left ventricle.

**SYMPTOMS.**—Many individuals present this lesion without being conscious of ill health. They may experience a certain amount of shortness of breath upon exertion, but do not suspect the existence of cardiac mischief. Some patients are of a tolerably fresh complexion and do not suggest the idea of cardiac difficulty, but rather of chlorosis; such patients, so far as the writer's experience goes, are rather slight and undersized. The great majority of sufferers are women. Some cases are supposed to be congenital, but this must

be exceptional. As compensation fails, we have the usual train of cardiac symptoms, with the difference that pulmonary engorgement, bronchitis, passive congestion of the lungs, orthopnea, and hemoptysis are more common with this than with other valvular lesions because of the direct way in which it impedes the pulmonary circuit.

The thrill in mitral stenosis is overrated. Prominence of the left auricle as a convexity of the heart dulness in the left 2d, 3d, 4th and 5th interspaces is of diagnostic aid. In doubtful cases exercise may enhance the murmur. When auricular fibrillation is superimposed, the presystolic phase of the diastolic murmur disappears and the early and mid-diastolic portions persist. A presystolic murmur simulating that of mitral stenosis may occur in an irritable or excited normal heart and in the thyroid heart. White and Reid (*Med. Clin. of No. Amer.*, iv, 283, 1920).

A presystolic murmur and thrill occasionally occur in large hearts with hypertension and beginning dilatation, in the absence of any organic defect. Irons and Jennings (*Jour. Amer. Med. Assoc.*, Apr. 1, 1922).

**DIAGNOSIS.**—As already stated, the disease may be unsuspected until a physical examination is made. Upon inspection of the chest, we may observe the apex beat displaced slightly to the left. The lower part of the sternum and the apex region may be somewhat prominent in children, and an impulse may be seen with the systole in the fourth and fifth left space, due to the hypertrophied right ventricle.

The writer has often noted pain and dulness in the right paravertebral region. Fluoroscopy may show the left auricle at the right border of the heart. Mentl (*Casop. lek. cesk.*, Apr. 26, 1924).

Upon palpation near the apex, usually somewhat inside of it, may be felt a re-

markable purring thrill, which will be found to be presystolic in time and to terminate with a distinct shock corresponding to the beginning of cardiac systole. This shock may be felt over three or four intercostal spaces to the left of the sternum. Its origin is a matter of considerable speculation, but not as yet of demonstration.

On percussion the cardiac area will be found to be increased transversely to the right of the sternum. On the left it often reaches somewhat higher than normal, but laterally not much beyond the normal limits.

On auscultation at or inside the apex is heard a presystolic murmur of a characteristic quality. It is more or less rubbing, rumbling, or churning, and terminates with a sharp valvular sound corresponding to the shock felt by the hand. Immediately following this sound, if the case is one of pure mitral obstruction, is a brief pause, and then a fainter valvular sound is heard, corresponding to the second sound of the heart.

A study based upon the results of simultaneous records taken by a microphone and a string galvanometer showed that in mitral stenosis the diastolic murmurs are due to the rapid outflow of blood through the stenosed mitral orifice. Murmurs occupy those periods of diastole during which the velocity of outflow reaches a certain grade. When the auricle contracts at the normal time and the heart beats slowly, the velocity tends to be greatest in presystole; otherwise it is usually greatest in early diastole, and these are the periods at which the murmurs are most commonly audible. Lewis (*Brit. Med. Jour.*, Dec. 21, 1912).

If the case is one of stenosis and regurgitation combined, the first sharp valvular sound is followed by a systolic murmur.

The character of the typical presys-

toxic murmur of mitral stenosis is so distinctive that it would seem to the writer possible to establish a diagnosis of mitral stenosis upon this sound alone without other evidence.

In all 36 cases of mitral stenosis were diagnosed from a draft increment of about 15,000 men, 24 being "pure" cases and 12 associated with insufficiency. Of etiologic factors in the 24 cases of pure stenosis examined by the writer, rheumatic fever, chorea, tonsillitis and growing pains were the most important. In some instances, rheumatic fever, chorea and tonsillitis appeared together. Cyanosis was observed 14 times and pallor 4 times in these cases. A presystolic thrill ending in the characteristic systolic shock was felt 22 times. In all of the 24 cases a murmur was heard, usually in the recumbent position, and always best in the ventral decubitus. A snappy first sound was heard typically 19 times; in the 5 cases in which it was not heard a systolic murmur, accidental or without significance, muffled it. Goodman (*Amer. Jour. Med. Sci.*, Jan., 1919).

At the base of the heart in the second left space is heard a sharply accented and usually reduplicated sound, corresponding to the closure of the pulmonary valves under tension.

In cases of failing compensation, the thrill may be difficult to feel. It may sometimes then be perceived by apposing the palm of the hand lightly to the chest wall, when a very faint and extremely circumscribed thrill may be detected. With a dilated heart the auscultatory sounds also are indistinct. It may be impossible to recognize the existence of mitral stenosis in a patient seen then for the first time. If, however, compensation be restored wholly or in part, the murmur may reappear. The time of the murmur may be post-diastolic or middiastolic rather than strictly presystolic. The pulse is small

and irregular. When compensation fails, it becomes weak, frequent, more irregular, and intermittent.

A study of pure mitral stenosis in 200 cases showed that incipient, rudimentary mitral stenosis escapes detection by ordinary inspection and palpation, but that it is possible to differentiate it even in its earliest stages by various signs and symptoms. These include the displacement of the wave of the apex beat to the left (which was found in 91 per cent.) or to the left and upward (5 per cent.); slight reduction in the passive mobility of the heart (55 per cent.); displacement upward of the apex when the patient changes from the reclining to the seated position (73 per cent.); the beat more extensive in the transverse sense (88 per cent.); the beat a little more pronounced than normal (7 per cent.); the beat arrhythmical (51 per cent.) or a double impulse at the apex (5 per cent.); absence of the physiologic negative pulsation (25 per cent.); diffuse shock in the lower half of the sternum; well-marked pulsation at the left and right margins of the sternum; cardiac impulse in the epigastrium (97 per cent.); in the lung region (33 per cent.); the auricular cardiac impulse of Grocco (15 per cent.); diastolic valvular shock over the pulmonary; presystolic or diastolic-presystolic thrill at the apex; Brun's dull pain at a point in the epigastrium, below and to the left of the xiphoid appendix, the continuous vague pain here being exaggerated by pressure and sometimes becoming sharp and radiating to the region around the umbilicus or the entire abdomen or in a girdle radiating to the lower part of the back; Vaquez's auricular tender point is the result of enlargement of the auricle. The pain here develops spontaneously at different points or can be elicited by pressure. The patient complains of vague discomfort in the back, but locates the seat of the pain on demand in the region between the spine and the spinal margin of the left scapula. In conclusion the writer expatiates on the great diagnostic importance of the zones of Head in differentiation of pure mitral stenosis, and gives the

details of 5 cases in which these zones were particularly in evidence. Landolfi (Jour. Amer. Med. Assoc., from *Riforma Medica*, April 27, 1912).

Tricuspid stenosis may give rise to a presystolic murmur, situated to the right of the sternum; but this disease is extremely rare unless congenital, and when it does occur is apt to be secondary to chronic lesions of the left side of the heart. Persons born with tricuspid stenosis are apt to be simultaneously affected with other abnormalities which entail speedy death.

The late Austin Flint called attention to the presystolic murmur frequently heard in cases of aortic regurgitation at the apex of the heart, and ascribed it to the influence of the blood-current falling into the left ventricle through the incompetent aortic valves. This murmur is associated with the ordinary signs of aortic regurgitation and is not accompanied by the peculiar thrill felt in mitral stenosis; nor is it followed by the systolic shock above described.

There are two valvular affections of the heart which may give the impression of an aortic aneurism. The first, aortic insufficiency, as Corrigan pointed out, suggests it by the marked pulsation of the arch of the aorta. To the paroxysms of cyanosis and dyspnea may be added a visible pulsation in the second left interspace close to the sternum and a paralysis of the left vocal cord. Ortner (of Vienna) was the first to describe the compression of the left recurrent laryngeal nerve between the aorta and a considerably dilated left auricle, in a patient in whom he had diagnosed aneurism *intra vitam*. The majority of the cases have such a cause, but some few are due to compression by enlarged pulmonary veins or the left pulmonary artery. The writer witnessed 3 cases, 2 of which were with autopsy. All 3 had signs of a double mitral lesion and paralysis of the left vocal cord. Autopsy in 2 of

the cases showed the recurrent laryngeal nerve sclerotic and opaque in the portion compressed between the wall of the left auricle and the aorta. Osler (*Arch. d. mal. crur., d. vaisseaux et d. sang.*, vol. ii, p. 73, 1909).

There are now on record 11 autopsied and 26 clinically reported cases in which recurrent laryngeal paralysis was associated with and apparently the result of mitral stenosis. Among the autopsied cases the vocal paralysis was attributed to direct compression on the part of the auricle or its appendix in 7; to cardiac displacement, traction, etc., in 1; to the effects of a persistently patulous ductus arteriosus in 2; and to indirect compression acting on the pulmonary artery in 2. Fetterolf and Norris (*Amer. Jour. Med. Sci.*, May, 1911).

In 12 cases of soldiers in whom presystolic murmurs were suspected, but in whom they could not be recognized with any degree of certainty, amyl nitrite (inhaled from a 3-minim (0.18 c.c.) capsule until a reaction was evident) brought forth unmistakable murmurs in 6 instances. The point emphasized is that amyl nitrite, in a large proportion of cases, will raise the scale of the signs, bringing them nearer to a point in which a diagnosis becomes certain. Morison (*Brit. Med. Jour.*, Apr. 20, 1918).

**ETIOLOGY.**—Rarely the lesion may be congenital. In most instances it is the result of valvular endocarditis due to rheumatism or chorea or some other of the children's diseases. Anemia and chlorosis have also been thought to have some influence in promoting its occurrence.

Pure mitral stenosis is an independent valvular defect which generally develops between the ages of 10 and 30 as a result of endocarditis. It may be congenital or functional, but only in the rarest cases. The female figure, especially when there is a tendency to weakness and hypoplasia, seems to favor the development of this form of valvular defect. It consequently occurs mainly in girls and is distinguished by its rela-

tive harmlessness, although the patients rarely live to an advanced age. Hampeln (*Deut. Arch. f. klin. Med.*, Bd. cv, Nu. 5-6, 1912).

**PATHOLOGY.**—Mitral stenosis is almost invariably associated with a greater or less degree of mitral regurgitation. By itself, mitral stenosis does not cause much enlargement of the heart. The left ventricle may be of normal size or smaller. The left auricle and right ventricle are, however, much dilated and hypertrophied. The valves may be changed to a variable extent. In the most extreme cases the auriculo-ventricular orifice is scarcely big enough to admit the head of a pin. The left auricle often contains thrombi. Sometimes the great enlargement of the left auricle causes pressure paralysis of the left recurrent laryngeal nerve—the same lesion which is caused, more often, by thoracic aneurism.

In a series of 50 cases which came to autopsy, the cardiac lesion was confined in 25 cases to the mitral valve; in 7 others the mitral lesion was the chief finding, but was combined in 2 with chronic fibrous pericarditis and in 5 with inflammation of the aortic valves. Aortic stenosis complicated 9 other cases, aortic insufficiency 3, and tricuspid stenosis 6. In 4 of the latter aortic regurgitation was also present. G. G. Sears (*St. Paul Med. Jour.*, March, 1907).

**PROGNOSIS.**—As already stated, mitral stenosis is not incompatible with a tolerable degree of health, and may not for years call attention to itself. Even after compensation has been impaired, great improvement may be repeatedly obtained by suitable treatment. On the whole, the disease may be said to be somewhat less favorable than is mitral insufficiency. Yet, of this, as of every cardiac lesion, it should be said that the prognosis depends upon the

peculiarities of the individual case, which should be considered upon its own merits.

**TREATMENT.**—The treatment is considered at the end of the section on VALVULAR DISEASES, page 500, to which the reader is referred.

### AORTIC REGURGITATION.

**DEFINITION.**—A lesion of the aortic valves allowing a reflux of blood into the left ventricle during diastole.

A patient with free aortic regurgitation may for years lead an active life unconscious of his condition. In no other valvular disease is compensation, while it lasts, so perfect. If, however, the lesion develops abruptly, it will produce marked symptoms. For instance, when it is consequent upon the sudden rupture of a segment of the valve during violent physical exertion, or when the valve is perforated by the ulcers of malignant endocarditis, the heart may be almost or completely overwhelmed by the sudden strain put upon it, the left ventricle dilating and thus causing relative insufficiency of the mitral valve, engorgement of the lungs, and an embarrassment of the whole circulatory apparatus, from which the patient can scarcely recover.

In some instances the first shock is successfully endured, and a slow development of the reserve power of the heart establishes compensation. This happier result was observed by the writer in the case of a Western miner in whom the aortic lesion developed overnight.

The commonly accepted view that mitral disease is by far the most frequent of the valvular lesions of the heart should be modified. From his experience in private practice, as well as with extensive hospital material, the writer believes that aortic lesions are fully as frequent or more so than lesions of the



mitral orifice. From the records of the Cincinnati Hospital for four years, from 1900 to 1903 inclusive, it was found that, in 160 autopsies with well-defined heart lesions, aortic disease and mitral disease were about equally distributed, with a slight margin in favor of the greater frequency of the former. Admitting that the infection, as seen in acute articular rheumatism, more frequently affects the mitral area, the fact remains that the severest type of the so-called ulcerative endocarditis does greatest damage to the aortics. Especially in syphilis, is the tendency to aortic lesions pronounced. J. E. Greiwe (Jour. Amer. Med. Assoc., March 9, 1912).

**SYMPTOMS.**—Where compensation has been perfect and is beginning to fail, the first symptoms may be cerebral, such as dizziness, flashes of light, and slight headache; there may also be faintness and palpitation on slight exertion. A patient seen by the writer had for his first symptom a sharp neuralgic pain in the lower jaw which developed while he was carrying a canoe on his back through the woods of Maine. Pain may be very prominent. It is usually precordial, but may extend into the neck and down the arms, particularly the left arm. Angina pectoris may occur, and in no form of valvular disease is sudden death more common than in this.

Compared with mitral lesions, there is less apt to be cyanosis, bronchitis, or anasarca: more apt to be head symptoms and pallor. Embolism may occur, and slight febrile attacks are not uncommon, either due to recurrent endocarditis or in some instances to articular rheumatism. In this and in other valvular lesions there may be delirium toward the close of life.

It is also stated that there seems to be some connection between mental diseases and cardiac lesions even when well compensated. With regard to this

the writer has had no practical experience. It is usually said that the cardiac psychoses are apt to be of a melancholy character. Savage says: "With aortic or with both aortic and mitral disease, the symptoms may be either melancholic or maniacal; but I am inclined to think that, with simple aortic disease and with hypertrophy of the left ventricle, it is at least not uncommon to meet with acute mania and exaltation of ideas."

Aortic regurgitation sometimes occasions cerebral hemorrhage, and pericarditis sometimes complicates disease of the aortic valves, whether stenosis or regurgitation.

Upon physical examination it is usually easy to recognize aortic insufficiency if it exists. Inspection shows an extensive and powerful cardiac impulse. The apex is seen to be in the sixth or seventh intercostal space in the nipple line or outside, and the chest wall may be prominent over the hypertrophied left ventricle. Upon palpation, the powerful action of the heart is evident, and exceptionally there may be a diastolic thrill. In this disease the heart may attain its largest dimensions.

In young adults the murmur of aortic insufficiency is generally heard to the left of the sternum, in the third interspace, instead of at the classic site as taught in the textbooks. The Röntgen rays will confirm the diagnosis of the aortic insufficiency in these cases. Only when the valvular trouble has reached an advanced stage and been aggravated by the dilatation of the right cavities, is the murmur heard at the classic site to the right of the sternum. This was the case only in 10 of 66 cases studied; in 26 the murmur was heard to the left of the sternum; in 20 at the sternum itself; in 9 at the xiphoid. When the murmur was heard at the left of the sternum it was usually either at the third or the second interspace.

Trémolières, Caussade and Toupet (Presse Méd., Aug. 9, 1917).

Upon auscultation, there is heard a diastolic murmur, which may be loudest in the second intercostal space on the right, or in the third or fourth space at the left edge of the sternum. Exceptionally it may be heard best at the left side near the xiphoid cartilage. This murmur is of low pitch, and of a blowing character, and it may replace the second sound of the heart. If not, it begins immediately upon the occurrence of that sound. No cardiac murmur is audible over so extensive an area as may be that of aortic regurgitation. It may be heard all over the chest, and in the brachial and femoral arteries. In some cases it is difficult of detection, and, when this or any valvular lesion is suspected, it may be laid down as a general rule that no examination is complete unless auscultation has been carefully practised when the patient was in a horizontal and also in a vertical position.

Sometimes the murmur can be heard best with the naked ear applied to the uncovered chest wall. Exceptionally the murmur may be heard only at the apex of the heart, and in this connection the murmur described by Flint, presystolic in time and heard at the apex, should be borne in mind. This has been already described in discussing the diagnosis of mitral stenosis. Flint's murmur is of a blubbery character, and heard only over a limited area at the apex. The sound heard at the base of the heart is usually rather long; when it is short and gushing there is (it is claimed) reason to infer an extensive lesion. It is stated that it is also unfavorable to find the murmur audible only in the midsternal region. Sometimes the murmur has a distinctly musi-

cal quality. This is explained as due to the perforation of a valve segment in such a way that a thin strip of valve is left intact and made to vibrate by the regurgitating blood. Frequently there is an accompanying systolic apex murmur, due to relative incompetency of the mitral valve, although, of course, it may be a sign of coexistent mitral disease. Usually there is at the base a systolic murmur, and this occurs independently of aortic stenosis. One explanation of its development is that the first outflow of blood from the contracting ventricle meets the still regurgitating current falling through the incompetent valve, and thus gives rise to the murmur.

The diastolic murmur may sometimes be heard, as already stated, in the peripheral arteries. Sometimes the second sound of the heart may be heard in the carotid when not audible at the base of the heart. If so, its interpretation is favorable as implying a lesser lesion of the aortic valves. Sometimes a systolic and diastolic murmur may be heard in the femoral and other arteries (Duroziez). This is obtained by a slight pressure with the stethoscope, and is due to the outward current of blood causing a systolic and the returning blood a diastolic sound at the place of artificial stenosis. This is a very important diagnostic factor when found, but it is not always present in aortic regurgitation.

The point of maximum intensity of the aortic diastolic murmur is not constant, but varies under different conditions, most authorities placing it in the third and fourth interspace to the left of the sternum and near its margin. The writers, having noticed the frequency of a diastolic murmur at the apex and in the axilla, made a careful study in a number of cases of aortic insufficiency as regards these points of

transmission. In all but 2 of 17 cases examined the diastolic murmur was heard outside the apex in the axilla. At times the murmur in the axilla may be of secondary or even as in 2 cases of maximum intensity, that is, in passing from the point of maximum intensity close to the sternal border, the murmur diminishes in intensity as the apex is reached and then becomes louder in the axilla. This axillary murmur is of exactly the same kind and quality as that heard at the base, and should be identified as the "aortic axillary diastolic" murmur, R. Cole and A. B. Cecil (Johns Hopkins Hosp. Bull., vol. xix, p. 353, 1908).

Aortic insufficiency without murmur can be diagnosticated by palpation, when the vaulting shock will be noted, that is, a dome-shaped elevation of the region of the apex at each aortic impulse without valvular vibration. LeBarb (Semaine méd., June 2, 1909).

Leonard Hill noted that in aortic regurgitation there is remarkable difference in systolic pressure found in the arm and leg, the pressure in the lower limb being often extraordinarily high, not rarely amounting to 100 millimeters of mercury above that of the upper extremity. The writer found, in making comparative studies of the blood-pressure in the arm and leg of cases of aortic regurgitation, not only confirmed Hill's conclusions, but gave even greater variations than he records, and that this extraordinary difference between the systolic pressure in the arm and leg is a pathognomonic sign of aortic incompetence, as it is not present in other valvular lesions. H. A. Hare (Therap. Gaz., July, 1910).

Systolic murmurs at the base of the heart when they are not followed by a diastolic murmur are generally inorganic. This was shown in 55 men with valvular defects who had been at the front for a few months up to 2 years and confirmed the great tolerance even the indifference of valvular defects in respect to the fatigues of

life at the front. Mitral stenosis is the least resistant, but even with this the men had nothing more serious than palpitations or transient attacks of tachycardia. Congenital and complex valvular defects seemed to do as well as any. One of the great elements of this tolerance is the fact that the men were not aware that they had valvular disease. A young man with a valvular disease should be assigned to light duty only. If over 35, and if there are pains in the heart, attacks of tachycardia and palpitation on exertion and the man has been sent back for recurring rheumatism or typhoid, the writer advises temporary discharge to refrain from compromising the man's future. C. Laubry (Paris Méd., Dec. 15, 1917).

The femoral artery, and also the smaller arteries, such as the dorsalis pedis and the radial, usually afford a peculiar, sharp, valvular "pistol-shot" sound with each cardiac systole. This sound may exceptionally be doubled.

The pulse is characteristic. It has been called the "water-hammer" pulse, or the "Corrigan" pulse, after Corrigan, who admirably described it, or the "shuttle" pulse. It is very quick and abrupt, and is extremely ill-sustained. These characteristics are more evident if the arm is raised vertically, and they can be well appreciated by grasping the wrist with the hand (Osler) instead of by the ordinary mode of palpation with the finger. In this disease there is also a capillary pulse; a phenomenon which may also be observed in neurasthenia and profound anemia, but much less often. It can be seen in the nails, in the vessels of the retina through the ophthalmoscope, upon a surface artificially reddened by firm rubbing, as on the forehead, and it may also be well observed through a glass slide placed upon the everted lower lip. It con-

sists of an alternate flushing and paling of the part, corresponding with the sudden filling and emptying of the vessels. Rarely, there is a venous pulse seen on the back of the hand.

**DIAGNOSIS.**—As already stated, persons may have aortic regurgitation without symptoms; hence the disease may sometimes be discovered only upon physical examination. When the signs above enumerated have been detected, the diagnosis is practically certain.

A diastolic murmur at the base of the heart may be occasioned by an enlargement of the aorta due to aneurism, but this lesion would have a different history and would present other signs peculiar to itself. Moreover, aneurism usually gives a systolic, rather than a diastolic, murmur. Examination with the X-ray would be conclusive.

Insufficiency of the pulmonary valves is a very rare lesion, and, if present, the murmur caused by it should be transmitted downward and to the right, and there would be no hypertrophy of the left ventricle or "water-hammer" pulse.

Patency of the ductus arteriosus is a rare condition, and the murmur associated with it has been described as "late systolic" or, again, as "continuous with the second sound, transmitted only very feebly to the left, and of a wavy character, sufficient of itself to distinguish it from an aortic regurgitant murmur."

The causes of degenerative lesions producing aortic regurgitation in old age are (1) senile degenerative change, (2) high arterial tension or constant strain on the valves and arch of the aorta, (3) severe intermittent strain on the valves from frequent and violent fluctuations in the blood-pressure, (4) syphilitic aortitis, (5) rupture of a valve.

The physical signs are sudden, short, and forcible pulse wave, high blood-pressure, hypertrophy of the left ventricle with a diastolic murmur at the aortic cartilage, the aortic second sound being also present and indicating dilatation of the aorta. Broadbent (*Practitioner*, March, 1908).

**ETIOLOGY.**—Aortic regurgitation is seen most often in middle-aged, vigorous men accustomed to considerable muscular exertion. Modern studies have shown that at least 75 per cent. of pure aortic cases are due to syphilis. It may also be caused by endocarditis, arteriosclerosis, gout, alcohol, etc.

Examination of 467 patients showed that: Syphilis is an important factor in the production of aortic regurgitation; 37.3 per cent. of all patients with aortic regurgitation between 20 and 70 show a positive Wassermann reaction. Rheumatism is of rather less importance and accounts for 27.2 per cent. of the cases. Pure aortic regurgitation is mainly a disease of middle life, from 40 to 50, while combined aortic regurgitation and mitral stenosis is essentially a disease of young people, under 30 years of age. Fifty per cent. of all cases of pure aortic regurgitation are syphilitic in origin, and 17.4 per cent. rheumatic. Between the ages of 20 and 35, 44 per cent. of cases of pure aortic regurgitation are rheumatic in origin and 10.7 per cent. are syphilitic. From 35 to 40, 14.3 per cent. of cases are rheumatic and 40.5 per cent. syphilitic, while over 40 years of age, only 5.2 per cent. of cases are rheumatic and 71.3 per cent. syphilitic. Syphilis is of most importance as an etiologic factor in patients over 35 years of age, because syphilitic aortitis, and hence aortic regurgitation, is not pronounced enough to cause cardiovascular symptoms until from twenty to twenty-five years have elapsed from the infection. Rheumatism is of most importance as an etiologic factor in patients under 35, because rheumatic fever is essentially a disease of young people and cardiovascular symptoms

due to rheumatism appear on the average 11.6 years after the attack of rheumatic fever. Syphilis and rheumatism are both of lesser importance in the causation of aortic stenosis (with regurgitation), syphilis accounting for only 20 per cent. and rheumatism for only 13.4 per cent. of the cases. Harmer (*Heart*, Mar., 1926).

Atheroma of the aorta may extend into and deteriorate the valves.

The valves may be congenitally affected. In most such cases they are still competent at birth; but they are apt to become impaired in later life.

Ulcerative endocarditis may produce a sudden incompetency of the valve, with great and perhaps fatal embarrassment of the cardiac circulation, as already mentioned. And, finally, sudden muscular strain may produce a rupture of one of the segments, especially if the valve is previously impaired by disease.

**PATHOLOGY.**—Besides the usual changes in the valves themselves, there are lesions peculiar to aortic regurgitation in the heart and blood-vessels. As already stated, the heart becomes enormously hypertrophied, weighing 40 to 45 ounces instead of 10 or 12. The main part of this increase is in the walls of the left ventricle, the cavity of which is enlarged, but its walls more than proportionately thickened. The muscular trabeculae of the ventricle are usually more or less flattened where the regurgitant blood-current impinges upon them.

While in all kinds of valvular lesions the heart is exposed to ultimate degenerative changes, this liability is particularly great in aortic regurgitation, because the coronary arteries upon which the nutrition of the heart wall depends, originating, as they do, at the base of the semilunar valves, no longer have a normal amount of blood forced

into them. Moreover, if the lesion of the valves is due to fibrotic changes, the orifices of the coronary arteries are apt to be involved in this process and more or less occluded. Hence those cases of aortic regurgitation have a decidedly better prognosis which are due to rheumatism than those which are associated with atheroma.

The systemic arteries become dilated by the large volume of blood which is thrown into them with each contraction of the enormous left ventricle, and they also undergo sclerotic degeneration because of the strain which they experience.

**PROGNOSIS.**—Aortic regurgitation is the most dangerous of the acquired valvular lesions of the heart. It is consistent with comfort and vigor lasting for years, but there is always the possibility of a sudden fatal termination; and when once compensation has been interrupted, it is seldom satisfactorily restored. Sometimes upon the development of secondary mitral insufficiency there will be a noticeable alleviation of the cardiac embarrassment, but the patient is relieved, not saved.

Pure aortic stenosis is not very common, but is more frequently met with in combination with aortic regurgitation, when the modification in the character of the pulse which it entails is of great diagnostic value. It is one of the least serious of the valvular lesions unless associated with degenerative changes in the aorta in later life. It is not progressive in the same degree as mitral stenosis.

The prognosis in mitral stenosis is always serious as regards duration of life, though the patient may survive a considerable number of years, as the tendency is for the constriction of the mitral orifice to be progressive. Broadbent (*Dublin Jour. of Med. Sci.*, April, 1909).

**TREATMENT.**—When the aortic valves are diseased from causes other than endocarditis, **iodide of potassium** in doses of 5 to 10 grains thrice daily given for long periods has been followed by great improvement. This is no doubt due to the fact that so many of these cases are syphilitic in origin. They should always be investigated with this point in mind, and, if found to be syphilitic, should be given vigorous antisyphilitic treatment. This applies to cases of stenosis as well as regurgitation.

Some writers have advised against the use of **digitalis** in aortic insufficiency, fearing the bad effect of lengthening the diastole and thus affording a longer time for regurgitation; but the weight of authority is undoubtedly in favor of employing **digitalis** when it seems to be needed, despite this theoretical objection.

By far the most important time for treatment is at the onset in rheumatic cases. Children with growing pains or a pain in any joint should always have their hearts examined—the onset of endocarditis is so insidious. During the acute stage **salicin** or **aspirin** given in full doses appears to be less depressing to the heart than salicylates. Small repeated **blisters** to the first, second, or third spaces on the left side, as recommended by Caton, are distinctly useful, as also is **potassium iodide** after the temperature has fallen. When the aortic valve is affected, **rest** in bed is essential, not only until the temperature comes down to normal, but for at least six weeks after, and then a very gradual return to being up all day, and no exercise or work should be allowed for six months or more. If so treated the murmur and all signs of the regurgitation will in rare instances completely disappear. This happened in a recent case under the writer's observation. But when the regurgitation persists, as it usually does, compensation is attained

with as little dilatation as possible, and so more reserve is left for future contingencies.

In syphilitic cases **potassium iodide** tends to prevent the increase of the lesion, and does good by lowering the vascular tension. Atheromatous cases need tonics combined with measures to reduce the peripheral resistance.

In all cases tonics such as **strychnine**, **arsenic**, **formates**, **ammonia**, and bark are most useful, and **belladonna** if there is palpitation. Hypodermic injection of **morphine** is the best hypnotic if the nights are bad.

If venous congestion or dropsy comes on, **digitalis** combined with vascular dilators and diuretics will be useful. Then, if the mitral and tricuspid breakdown was due to the amount of the aortic regurgitation, the **digitalis** must be at once stopped, since it is a dangerous drug to use in aortic regurgitation. Broadbent (*Lancet*, Nov. 12, 1910).

In failing compensation in aortic insufficiency, the writer advocates the continued use of **squill**, 0.3 Gm. (5 grains), eventually reduced to 1 such dose a day. Other drugs, *e.g.*, **codeine** or **theobromine sodiosalicylate**, may be also used if necessary. Mendel (*Berl. klin. Woch.*, Nov. 21, 1921).

Extensive war experience has convinced the writer that an aortic diastolic murmur between the ages of 40 and 50 is nearly always of syphilitic origin. Even without any other evidence he advises **neoarsphenamin** and **potassium iodide** treatment. Amblard (*Bull. méd.*, Feb. 18, 1922).

Further suggestions will be found under TREATMENT OF VALVULAR DISEASES, at the end of this section, page 505.

## AORTIC STENOSIS.

**DEFINITION.**—A lesion of the aortic valve obstructing the normal flow of blood from the left ventricle into the aorta.

**SYMPTOMS.**—Well-compensated aortic stenosis may last for years without subjective disturbances. When

compensation begins to fail, the pulse may become very slow, even as slow as 50 to 25 beats a minute, and there is a great tendency to dizziness, faintness, syncope, and epileptiform attacks. The subjects are frequently syphilitic. In elderly persons the lesion is generally due to simple arteriosclerosis. Upon inspection, the heart's apex may be seen downward and to the left from its normal position; but in some instances, when there is pulmonary emphysema or an unyielding chest wall, no cardiac impulse can be seen or even felt.

Percussion may show some enlargement of the left ventricle. Change in the right side of the heart does not ensue until the later stages of the disease.

Palpation very often detects at the base of the heart on the right side a distinct rough, systolic thrill.

Auscultation discloses a rough, long-drawn, systolic murmur, heard best in the second right interspace, of a sawing character, and transmitted into the carotids. It is followed by the second aortic sound, unless there is also a diastolic murmur, when the latter may supplant the normal valvular sound. Often there is accentuation of the second aortic sound, particularly if there be chronic degenerative changes in the kidney.

The murmur is not invariably harsh. It may exceptionally be soft and blowing, or even musical.

**DIAGNOSIS.**—A systolic murmur at the base of the heart may be heard in anemia, but this is usually in young subjects, and loud upon the left as well as upon the right side of the sternum, and it is not accompanied by the characteristic thrill nor by hypertrophy of the left ventricle. A

systolic aortic murmur is heard very frequently in connection with the murmur of aortic regurgitation independent of any stenosis. This murmur is comparatively soft in character and unaccompanied by thrill. A systolic murmur may be heard in the aortic region caused by roughening of a calcified aorta without the existence of stenosis. Here we would fail to find enlargement of the left ventricle, or the peculiarly slow, infrequent pulse of stenosis. The systolic bruit of a thoracic aneurism, heard in the same region, would be accompanied by pain, dilating tumor, X-ray shadow, and other signs of the true condition, and not associated with the peculiar pulse or with any hypertrophy of the left ventricle unless there were coexistent aortic regurgitation. A mediastinal new growth may press upon the aorta in such a way as to cause a harsh systolic murmur, but without any necessary sclerosis of the arteries, as seen in aortic stenosis, and with a tumor to be detected by percussion and by the X-ray. Moreover, the blood-count might aid here in diagnosis.

The systolic murmur of pulmonic obstruction and that of patent ductus arteriosus are not transmitted into the systemic arteries.

**ETIOLOGY.**—In some cases the valves appear as if the lesion might have been congenital, but almost always the disease develops late in life, and is a slow, fibrous, and calcareous change in the valves associated with degenerative changes in the whole arterial system. The left ventricle is slightly dilated, but mainly hypertrophied.

**PATHOLOGY.**—Sometimes there is a subvalvular stenosis because of

fetal endocarditis. There may be vegetations on the valves due to endocarditis. Usually the lesion is sclerotic or calcareous. The coronary arteries may be involved, resulting in myocardial degeneration.

**PROGNOSIS.**—The prognosis is comparatively favorable. Good health may be enjoyed for many years. When compensation begins to fail, sudden death, with cerebral symptoms, may occur.

**TREATMENT.**—Iodide of potassium in small doses, long continued, may be of great value.

For further suggestions the reader is referred to TREATMENT OF VALVULAR DISEASES, on page 505.

### TRICUSPID REGURGITATION.

**DEFINITION.**—Insufficiency of the right auriculoventricular valve.

**SYMPTOMS.**—The symptoms of tricuspid regurgitation are those seen in most cases of ruptured compensation, in valvular lesions of the left side of the heart, provided the patient lives long enough. They are headache, dizziness, indigestion, scanty urine, uneasiness in the right hypochondrium, wakefulness, cyanosis, anasarca, and orthopnea. Sometimes there is a peculiar greenish coloration of the skin, due to a slight icteric hue mingling with the cyanosis.

On physical examination we find by inspection a marked epigastric impulse, and by percussion a very extensive dullness to the right of the sternum. The characteristic murmur of tricuspid regurgitation is a soft, low, systolic murmur, heard best at the left edge of the sternum between the fourth and sixth ribs, and transmitted toward the right. It is seldom audible above the third rib. The in-

competency of the tricuspid valves causes dilatation of the subclavian and cervical veins, and when this has become so great that their valves are no longer competent the veins pulsate with every systole of the heart. This pulsation may be seen sometimes even in the axillary, thyroid, and mammary veins. The same systolic centrifugal impulse is also transmitted downward into the liver, and this organ may exhibit an expansile pulsation with every cardiac systole.

Heinrich Stern, in 1910, called attention to a new posture which he found of value in detecting tricuspid regurgitation, of inducing the characteristic murmur of this disease when it has been absent, and making it more distinct when it is vague and indistinct. When a patient is in the recumbent posture, if the head is lowered, the jugular veins become distended, and as a rule begin to pulsate. If the head is lowered beyond a certain degree, the pulsation and engorgement recede. This lowering of the head stretches the muscles of the head and also the jugular veins. This stretching is reflected in the tricuspid area, and murmurs are now evident which were not heard before, or which were quite indistinct. Sachs (Med. Record, Feb. 10, 1912).

The systolic murmur caused by tricuspid insufficiency is best ausculted between the ensiform and the left costal margin with the patient lying on the right side and in deep inspiration. When the right ventricle is dilated and hypertrophied, palpation in the same area is also particularly enlightening. Harzer (Deut. Arch. f. klin. Med., Oct. 26, 1920).

**DIAGNOSIS.**—The systolic murmur of mitral regurgitation is heard upon the left side of the sternum; as a rule, loudest at the apex, and transmitted toward the left axilla. If both the mitral and the tricuspid valves are incompetent, usually upon careful use



of the stethoscope an area can be found, going from left to right, where the mitral systolic murmur ceases, and on farther advance toward the right an area where the tricuspid murmur begins. Moreover, the latter murmur may be different in pitch and quality from the mitral murmur.

In a certain number of cases, it is possible to exclude tricuspid insufficiency, notwithstanding the existence of the jugular-ventricle pulse. These are the cases in which the jugular pulse is so weak that it is scarcely recognized as such, but the pulse is of the permanently irregular type, there are no signs of stasis and there may be absolutely no heart murmur. These features of the case exclude tricuspid insufficiency. Only when the jugular-ventricle pulse is pronounced should it be suspected. Hering (*Med. Klinik*, Sept. 19, 1909).

**ETIOLOGY.**—Tricuspid incompetency is usually secondary to dilatation of the right ventricle because of obstruction in the pulmonary circuit. This may be due to chronic bronchitis, pulmonary emphysema, fibroid induration of the lungs, or to mitral disease. Of these two classes of causes, the pulmonary are said to be of more unfavorable prognosis. Also, tricuspid regurgitation may be directly due to endocarditis. This may exceptionally affect primarily and alone the tricuspid valve, but it is mostly secondary to trouble upon the left side of the heart. If the endocarditis is ulcerative, there may be secondary pulmonary abscesses.

**TRICUSPID STENOSIS.**—Tricuspid stenosis is an extremely rare condition, causing obstruction of the right auriculoventricular valve. It may be congenital, in which case it is associated with other lesions, so that the patient seldom lives long. If acquired, it is almost invariably asso-

ciated with other valvular lesions, particularly mitral stenosis.

Its symptoms are cyanosis, sensitiveness to cold, dyspnea, and palpitation. A presystolic thrill has been observed, and a presystolic murmur, heard best at the base of the xiphoid cartilage or toward the right from that point.

The diagnosis of tricuspid stenosis is very difficult. In a table of 117 cases, by Lendet, it was made out during life only 6 times. The lesion is almost always combined with mitral stenosis, and both usually result from rheumatism. The patients are mostly females and rarely more than 40 years old. With the usual signs of mitral stenosis are associated, when combined with the tricuspid lesion, a feeble thrill and murmur over the sternum. The enlarged auricle is also likely to be notably enlarged, and before the heart breaks down there is likely to be subcutaneous dropsy, turgidity of the jugular veins, cyanosis, and dyspnea. The prognosis is very bad in congenital cases, children seldom exceeding the fourth or fifth year. In the acquired disease the average duration of life is 35 years. Crawford (*Pract.*, Feb., 1907).

Stenosis of the tricuspid orifice can hardly ever be recognized by the usual clinical means of investigation; when graphic methods are employed its presence can be determined positively. In reference to his case, the points to be noted are: The tracings obtained proved conclusively the presence of a tricuspid stenosis. Most likely there was also a mitral lesion, because of the systolic murmur transmitted to the left and the extensive enlargement of the heart to the left. Felberbaum (*Med. Rec.*, Aug. 28, 1909).

Tricuspid stenosis is often due to endocarditis following rheumatism, or some other acute infection. The fact that it is almost invariably accompanied by lesions of the mitral or aortic valves confirms this view. Osler states that congenital cases are not uncommon; they are usually accompanied by some

other defect. But there are also cases of congenital origin. These congenitally defective valves are undoubtedly very liable to postnatal endocarditis. The conspicuous symptom is the extreme cyanosis in the majority of cases. This is due to the marked venous stasis resulting from the tricuspid narrowing. Occasionally it has been absent. Otherwise, there is nothing characteristic. Dyspnea may be extreme when broken compensation, due to overdilatation of right auricle, supervenes. It is surprising with what degree of comfort these patients are enabled to go about for years. T. B. Fletcher (*Amer. Jour. Med. Sci.*, Nov., 1911).

The etiology and pathology are not different from those of the more common valvular lesions.

The prognosis is very unfavorable.

**TREATMENT.**—This is important in the sense that the prognosis will depend upon the severity of the back pressure and the power of response to measures of relief. These measures should aim more at the relief of resistance than at increasing the power of the heart. The heart needs soothing and rest, and if these are obtained relief for a considerable period may result.

### **PULMONARY STENOSIS.**

**DEFINITION.**—(Obstruction of the pulmonary valve.

**SYMPTOMS.**—This condition is almost invariably congenital, and it is usually associated with other structural anomalies, such as persistence of the foramen ovale and of the ductus Botalli, and defects in the septum ventriculorum. Most cases come to an early termination. Life is seldom prolonged beyond fifteen years. The marked symptoms are cyanosis, dyspnea, clubbing of the ends of the fingers, and deficient bodily development.

Upon auscultation we hear a loud systolic murmur over a rather extensive area, but loudest in the second left interspace, and sometimes accompanied with a systolic thrill. The pulmonary second sound is weak or absent, or it may be replaced by a diastolic murmur. The systolic murmur is not transmitted into the arteries of the neck, but in some cases seems to extend toward the left shoulder.

**DIAGNOSIS.**—It should be borne in mind that functional systolic murmurs may be heard in the second left interspace. They can be distinguished by the other physical signs and the age and general appearance of the patient. And it should also be remembered that sometimes the murmur of mitral regurgitation may be heard along the left edge of the sternum; but the latter murmur may also be heard in its usual position near the apex or in the back near the angle of the scapula. Moreover, the general symptom-complex would doubtless aid in distinguishing the true lesion.

In 3 cases reported by the writer mitral lesion so raised the pulmonary artery blood-pressure that that vessel and along with it the pulmonary orifice dilated and a murmur occurred, which appeared periodically in 2 of them over a period of years. These 3 cases are examples of the so-called Graham-Steell murmur. In 2 other cases cited no such cause seemed to exist, and probably the leakage was more due to relaxed tissues about the pulmonary orifice than to any marked increase in the blood-pressure of the pulmonary artery. A pulmonary systolic murmur, the commonest of all functional bruits, probably depends on a dilatation of the pulmonary artery, and in most cases tends to disappear. When, however, the dilatation involves the pulmonary orifice so that a diastolic leakage occurs the condition is of more import, although

even yet it may completely clear up. Rudolf (Amer. Jour. of Med. Sci., Sept., 1911).

**ETIOLOGY.**—Acquired pulmonary stenosis is rarely met with; the few instances on record being ascribed to acute rheumatism, acute infective diseases, and septic states, such as puerperal fever. Practically all cases, as previously stated, are congenital.

**PROGNOSIS.**—The prognosis is always unfavorable. Besides the impending cardiac failure, such patients are notably predisposed to pulmonary tuberculosis.

**TREATMENT.**—As to treatment, bronchial catarrh must be avoided, a dry and warm climate must be selected, and great exertion must be avoided. In general, the treatment must be symptomatic, on the lines applicable to cardiac failure, all indications for which are given below.

#### **PULMONARY REGURGITATION.**

Pulmonary regurgitation is deemed an excessively rare valvular lesion which is said to be accompanied by a diastolic murmur heard best over the pulmonary area, and transmitted downward and toward the xiphoid cartilage. It is usually associated with pulmonary stenosis or with some lesion on the left side of the heart. As distinguished from aortic regurgitation, it does not present the arterial and capillary symptoms of that disease, nor the striking hypertrophy of the left ventricle.

High pressure in the pulmonary artery may give rise to a functional leak in the pulmonary valves (Graham Steel, Barr, Gibson, and others). For instance, this may be heard in some examples of mitral stenosis. In this

case we have the picture of the principal organic lesion to show us the proper diagnosis.

Pulmonary regurgitation is the rarest of all heart lesions, and one which is not often detected during life. It may originate in disease or defect of the valves themselves, or in dilatation of the pulmonary orifice, and of the artery as well, without abnormality of the valves. It may be either structural or functional, the latter being more frequent than the former. It is more frequently associated with mitral stenosis than with any other heart lesion. It is also associated with emphysema. The condition is subsequent to the dilatation of the infundibulum of the right ventricle. There are no indications for treatment of pulmonary regurgitation different from those which are applicable to valvular disease in general. Crawford (Practitioner, Oct., 1907).

**TREATMENT OF VALVULAR DISEASES.**—Our first effort must be to promote and maintain perfect compensation of the valvular lesions. Our most important means to this end is control of the diet and of the bodily and mental activities. The diet should be **simple, nutritious**, easily digested, and the amount taken at any one time should be moderate. A considerable proportion of nitrogenous elements is desirable; sugar and starchy foods should be used sparingly. Thirst should mainly be quenched with pure water; this, again, is better taken frequently in moderate amounts than in excessive draughts. Tea is to be forbidden. Coffee may be enjoyed in moderate quantity if its effects do not prove unfavorable. Cocoa, milk, soups, and broths are suitable elements of the diet. In elderly and feeble persons, and in those previously habituated to its use, a moderate amount of alcohol may be advantageous; but, in general, its daily employment is harmful. Mental strain,

overwork, worry, and excitement, even if pleasurable, shorten the prognosis of comfortable existence.

The writer advises a **light, nutritious diet**, with a fair allowance of meats, fruit and vegetables, and not much starchy food. Not more than 2 pints of fluid a day should be taken. A **warm, dry climate** is best. A fair amount of **exercise**, short of actual fatigue, is beneficial, though if there is any indication of loss of compensation of the right ventricle, **rest in bed** should be at once adopted. In the medicinal treatment, he advocates **decalcifying agents**, such as the soluble salts of **phosphoric** and **citric acids**, as calcium promotes formation of fibrous tissue and the cementing together of the edges of the mitral valve, and also promotes separate rhythm of the right and left ventricles by reducing the irritability of the latter. Small doses of **calomel**, **colocynth** or **salines** are also given, and, when the heart-action is labored and the pulse rather frequent, small doses of **pilocarpine**, frequently combined with phosphoric acid and small doses of **strychnine** or **compound syrup of hypophosphites**. Small doses of **iodine** or **thyroid** are beneficial where the thyroid gland is inactive. For hemoptysis, **nitroglycerin** and **atropine** are used, and astringents condemned. To clear out stagnant blood in the air cells, **turpentine** is best. In cardiac thrombosis and pulmonary embolism with urgent symptoms, strong **ammonia** should be freely used. A mixture of 3 minims (0.2 c.c.) each of **aqua ammoniæ fortior** and **spiritus chloroformi** in a wineglassful of barley water every hour is effective. **Digitalis**, **strophanthus**, **squill**, **caffeine**, etc., should be used only during periods of cardiac failure. Sir James Barr (N. Y. Med. Jour., May 16, 1923).

Physical exercise is harmful unless its kind and amount be most carefully determined in each individual case, and—above all—its effects alertly observed for future guidance. The moderate employment of many muscles

is, of course, much better than the undertaking of special feats of strength. Walking and horseback-riding are suitable. Golf can be recommended for many patients with moderate lesions. Facing a high wind may be harmful to cardiac patients. When ordinary exercise is no longer wise, **massage** and **passive movements** may be of great benefit; also **stimulating baths**, as those of Nauheim. Many patients are anemic, and are benefited by **iron**, and others by **arsenic**; but this latter drug should not be used where there is any suspicion of tendency to fatty degeneration. Cases which evince a liability to pulmonary disturbance (especially mitral diseases) should be guarded against exposure to cold and wet.

If sudden cardiac failure develops, particularly in mitral cases, the **abstraction of 10 or 20 ounces of blood** from a vein may save life. If the symptoms are less urgent, analogous relief may be obtained by a **purge**, in which case **calomel** seems particularly efficacious.

In mitral regurgitation and also in tricuspid regurgitation, two main lines of treatment are indicated, *viz.*, to reduce resistance in the vessels and increase the power of the heart.

There are cases, commonly those in which dropsy is not prominent, in which the strain on the right heart is so great that the patient is livid and on the verge of suffocation; then **early venesection**, followed by diffusible stimulants, such as **ammonia** and **ether**, offers the best chance. Acute distress of this kind in tricuspid regurgitation is nearly always attended by two dangerous auxiliaries, sleeplessness and vomiting, directly due, in each case, to venous stagnation. Sleep must be obtained, and at times at any price. **Morphine** may be given most safely in the form of suppository, but

if given subcutaneously it may be advantageously combined with **strychnine**. Crawford (Practitioner, June, 1907).

When the signs of failing compensation are more gradual, our best remedy is complete **rest in bed**. A fortnight or two thus spent may fully restore compensation, independently of any drugs.

The treatment of *mitral stenosis* in childhood is mainly the treatment of rheumatism. The parents should be warned of the meaning of sore throats, fleeting pains, nervousness and chorea, feverishness and pallor. If possible such children should be taken from damp, low-lying houses, and properly clothed and their extremities protected. Large unhealthy tonsils should be enucleated. Spring and autumn, and particularly sudden damp cold after much heat, should be a signal for added watchfulness. Early symptoms should be promptly treated by **rest** and **warmth** and the use of **sodium salicylate**. F. J. Poynton (Clin. Jour., July 21, 1909).

In *mitral stenosis* it is not necessary to employ any medication having a special action on the heart and circulatory system, so long as compensation is fairly good and the central organ is doing its work efficiently. It is when the heart is flagging that special treatment is called for. A long **rest in bed**, say for a month, will often restore a laboring heart to an efficient discharge of its work. But the time comes, sooner or later, when compensation fails, and more energetic measures are called for.

Rest in bed is again one of the best aids to recovery in these cases. In the earlier stages of cardiac failure, the freshly made infusion of **digitalis** is the most reliable, given in full doses for three or four days, while the patient is resting in bed.

**Convallaria majalis** has certain advantages, in that it has no cumulative effect, and does not so readily produce nausea as does **digitalis**. It is well to commence with small doses (10 minims—0.6 c.c.) of the tincture. **Strophan-**

**thus** in the form of tincture may be prescribed in doses equal to those of the tincture of **digitalis**. It is especially valuable as a cardiac stimulant before edema has commenced.

There comes a time when the heart ceases to respond to any of these remedies when used singly. Then all three, **digitalis**, **convallaria majalis**, and **strophanthus**, are combined, and give remarkable results.

When stenotic patients have hemorrhage from the lungs, nothing should be done to arrest it provided it is not excessive. It is evidence that the patient ought to have been treated by **bloodletting**. Taylor (Practitioner, Aug., 1912).

A combined solution of **French digitalin**, 0.1 mgm. ( $\frac{1}{50}$  grain), and **ouabain**, 0.2 mgm. ( $\frac{1}{25}$  grain), in 0.75 c.c. (12 minims) of fluid, known as **digibain**, proved successful in some advanced heart cases. The amount referred to, or 1 c.c. (16 minims), was injected intravenously.

Among the cases reported by the writers was 1 of mitral stenosis and myocardial insufficiency refractory to other measures, in which intravenous, followed by oral, use restored and kept the patient relatively well. Laubry, Routier and Giroux (Bull. Soc. méd. des hôp. de Paris, Feb. 8, 1923).

In cases which have advanced still farther downward, either in spite of or before our ministrations, the treatment becomes the same as that indicated in dilatation. Briefly, this consists of absolute **rest in bed**, or if he cannot lie horizontally, in a chair. The **diet** should be bland but include viands, eggs, fowl, and gruel. Alcohol and wines should be kept for emergencies. Laxatives and even purges are very helpful, acting sometimes like venesection, in relieving engorgement. **Blue mass** or **calomel** followed the next day by a saline prove most satisfactory. Equal parts of **potassium bitartrate** and **jalap powder** 1 to 2 tea-

spoonfuls are also effective. To sustain the heart, our best stimulant is **digitalis**. This is indicated only when the heart's action is feeble and ineffective, particularly if rapid and irregular. A complete study of the therapeutics of **digitalis** and particularly in its relation to valvular disorders will be found on page 109 of the present volume.

If there is considerable dropsy, **digitalis** will work to much better advantage if preceded by free purgation with **calomel**, **blue mass**, or a concentrated solution of **sulphate of magnesia**. The mercurials seem to possess a peculiar power of dilating the arterioles, which other purgatives do not have. **Digitalis** is much more effective if great bodily quiet is enforced during its administration. If given at all, its dose should be such as experience finds suitable in the particular case in hand. If an ordinary dose does not seem to be of much benefit, gradually increasing amounts should be given until either there is improvement in the pulse or some toxic effect appears.

Nausea and diminution in the amount of urine are signs that **digitalis** had better be omitted. Some excellent observers believe that better results can be obtained from the use of the **digitalis** leaves, or an **infusion** made from them, than from the tincture. An easy way to obtain a fresh infusion for the patient is to order powders of **digitalis**, each one of sufficient size to make an infusion for twenty-four hours' use. No alkaloid of this drug appears to represent all its beneficent powers. In some instances, where there was obstinate vomiting, **digitalis** has been given with advantage by **enema**. When the heart appears to

have come under its influence, we must be prepared to interrupt its administration as soon as there is any diminution in the secretion of urine or tendency to nausea or to a fresh irregularity of the pulse.

If **digitalis**, after a careful and persistent trial, proves unavailing, recourse may be had to tincture of **strophanthus**, **caffeine**, **sparteine**, **adonidin**, or **convallaria majalis**; but, unfortunately, these are seldom of great advantage. **Strychnine** is a valuable, general, and cardiac tonic. It may be used to supplement other treatment, and also subcutaneously in case of dangerous collapse.

**Nitroglycerin** will often give great relief to cardiac distress and to dyspnea, particularly where the pulse is hard or where there is cyanosis.

In case of marked dropsy **diuretin** will sometimes prove very valuable. Another suitable remedy is a pill composed of 1 grain each of **squill**, **digitalis**, and **blue mass**, administered three times a day. If the kidneys are practically intact, **calomel** may be administered as a diuretic in the dose of 3 grains every three hours until effect: either decided purging or marked diuresis. The likelihood of purging may be diminished by combining, with this dose of **calomel**, **opium** in the amount of  $\frac{1}{2}$  to 1 grain. In case there is a considerable collection of fluid in serous cavities **aspiration** may give great temporary relief and enable the heart to recover some of its lost power; and when the legs are extremely edematous, the use of **Southey's tubes** or **scarifications** under antiseptic precautions may be of great service.

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**ENDOMETRITIS. — DEFINITION.**—Endometritis is an inflammation or hyperplasia of the uterine mucous membrane involving, to a greater or less extent, the parenchyma of the uterus.

**VARIETIES.**—Both in a clinical and a pathological sense, it is convenient to divide the disease into two varieties, viz.: (1) *interstitial* or septic endometritis, and (2) *glandular* or functional endometritis, or hyperplasia. Either of these two varieties may exist in the *acute* and *chronic* form, but the chronic form may follow a mild and overlooked acute attack, or may supervene in a gradual manner without being preceded by a recognizable acute attack.

Another *chronic* form affects the upper portion of the cervix at or contiguous to the internal os.

**SYMPTOMS.**—The symptoms may be divided into (1) disturbances of the sexual functions, (2) intermenstrual discharges, (3) pain and discomfort in and about the uterus or radiating from the uterus, (4) reflex disturbances, and (5) general symptoms.

Menorrhagia is one of the most frequent symptoms in the early stages, and in the *glandular* variety it often persists for a long time as the most prominent one. The flow may be moderately increased in amount or be a profuse hemorrhage with the passage of clots; it may be prolonged or may recur too often. In the later stages of *septic* or *interstitial* endometritis the menses are sometimes scanty. In certain acute attacks the menstrual flow is suppressed.

Dysmenorrhea is common in cases connected with flexion, puerile cer-

vix, or inflammation of the appendages.

Dyspareunia and sterility may be present under the same conditions.

Leucorrhœa is usually noticeable in the glandular variety and in the early stages of the septic. In the former the corpus secretes a thin, and the cervix a thick, clear mucus, both of which may be transformed into minute white coagula, at the external os, by the acid vaginal secretion, and appear at the vulva as a white or greenish-white discharge. In some cases the corporeal mucus is intermittently tinged with blood. The leucorrhœa may last throughout the month or only for a few days after the cessation of the monthly flow. In the septic variety the discharge is at first purulent, but later becomes mucopurulent. In cases of long standing cervical mucus may become exceedingly viscid when it is retained in the enlarged cervical glands, and gathers into a large, tenaciously adherent lump or plug at the external os. It sometimes has a disagreeable odor when it reaches the vulva.

Pain may be felt in the sacral or lumbar region, and may extend across the back or up the spine to the occipital region, or down the course of the sciatic nerve. Cutting or cramping pains across the lower abdomen or pubic region may be complained of, depending upon painful uterine contractions due to the expulsion or attempted expulsion of uterine discharges. Irritability of the bladder or rectum, or pain in the vagina or pubic bones, may be prominent. Feelings of weight in the vagina, and sensations as of prolapse of the pelvic organs are present

in some cases. Intercostal neuralgia is not uncommon.

Menstrual pain of a burning or aching character may be felt in the pelvis and back, or the pain may be suprapubic and colicky. It may last one or more days or throughout the period, and even for several days afterward. When the mucous membrane is exfoliated the uterine contractions are frequent and excessively painful, and last until the membrane is expelled.

Gaseous distention of the intestines, constipation, impaired digestion—with its accompanying reflexes, photophobia, and pain in the eyes after prolonged attempts at reading—are the ordinary reflex disturbances. Mental depression, worry, and the various manifestations of hysteria and neurasthenia are sometimes classed among the reflexes, although they are, as a rule, largely dependent upon other conditions and circumstances.

Chills, fever, and the other general symptoms of inflammation and sepsis are observed in acute endometritis.

In chronic cases anemia and nervous debility are often present, and seem to favor the development of reflex symptoms.

In the chronic endometritis which affects the upper portion of the cervix at or contiguous to the internal os the internal os dilates only slightly, its lumen is crowded with swollen and obstructed glands, and the circulation is interfered with at first by the pressure from within, and later by pressure from without due to a contracting band of inflammatory exudate. On account of such interference resolution does not take

place to the same extent as below, and a ring of imperfectly organized connective tissue remains whose upper edge is at or just above the os and whose lower edge merges into the somewhat thickened mucous membrane below it. In multiparæ this band does not necessarily interfere with uterine drainage, but in nulliparæ it usually takes on some of the characteristics of stenosis.

The diagnosis made by means of the sound is confirmed by the results of the treatment, viz., the disappearance of the physical signs and the relief of subjective symptoms such as backache, headache, reflex stomach disturbances, malaise, dysmenorrhea, menorrhagia, intermenstrual pain, and sterility. The number and severity of the symptoms vary greatly in different cases. Some patients do not complain of many symptoms although chronic inflammation in this location produces more subjective symptoms than inflammation in any other part of the uterus. Its symptoms are often attributed to a corporeal endometritis when such a condition is not present.

In all cases of chronic cervical endometritis or supposed corporeal endometritis a search should be made for induration about the internal os. The first and most noticeable sign in all but the most chronic cases is pain produced by slight pressure of the sound. When the os is anatomically small or is flattened by flexion, the pressure is not painful until it causes some dilatation or straightening or at least until it becomes firm. When the sound is passed through an inflammatory constriction with slight pressure, its withdrawal is followed by a show of blood at the internal os



or by a stain of blood on the sound. That the tenderness is primarily at the internal os, and not due to a general intrauterine tenderness, is evident from the cessation of the pain almost as soon as the bulbous end of the sound has passed the internal os. When the constriction does not interfere with the passage of the sound a little gentle manipulation can be made to locate the tender area at the internal os. When the ordinary uterine sound thus passes without encountering resistance, a series of graded sounds which taper slightly at the end are necessary both for the diagnosis and the treatment.

In some cases the ring of exudate can be traced by the uterine sound around the entire circumference; in others, a part of the circumference will have no ridge but is flat, smooth, and of a cicatricial hardness indicating partial or complete local destruction of the mucosa.

**DIAGNOSIS.**—Endometritis must be differentiated from angioma, tuberculosis, carcinoma, and myoma of the uterine mucous membrane.

Besides the symptoms, tenderness of the uterus, as evidenced by bimanual palpation, and sensitiveness of the endometrium at the internal os and fundus, as demonstrated by the passage of the sound, are of diagnostic value. The withdrawal of the sound may be followed by a slight flow of blood or mucus.

It is difficult to distinguish **angioma** from hemorrhagic glandular endometritis, except by the aid of the curette, which, in the latter case, will bring out some of the hyperplastic mucous membrane.

In **tuberculosis** of the endometrium the curette will find necrotic,

cheesy particles, and, perhaps, tuberculous tissue. An accompanying bilateral salpingitis and pelvic peritonitis with encysted ascites, particularly in virgins, indicate the condition. Tuberculosis elsewhere and a slowly progressive anemia add probability.

In **carcinoma** and **sarcoma** watery discharges, fetor; gradually increasing, intermittent metrorrhagia; rapid progress, and the microscopic examination of the findings of the curette are diagnostic. Carcinomatous infiltration of the cervix produces a globular enlargement that affects the supravaginal portion as much or more than the vaginal. Carcinomatous ulceration is excavated, fissured, pale red or grayish, with vascular spots that are friable and bleed easily upon being touched. A tenaculum tears it easily and causes abundant hemorrhage, but will hold firmly in an inflamed cervix. When there is cystic degeneration the tenaculum may tear out easily, but it causes a flow of mucus from the lacerated follicles with or without some hemorrhage. The inflamed cervix is usually soft and elastic; the carcinomatous, either hard or friable. Carcinomatous ulceration of the cervical cavity is excavated, dark or dull gray in color, bleeds slightly when touched, and conveys a slight odor to the cotton with which it is wiped.

Small intra-uterine and submucous **myomata** usually cause marked enlargement of the uterine cavity, and can sometimes be felt by the sound. Digital examination of the endometrium through the dilated and incised cervix is of great value in discovering this, as also other conditions, al-

though the procedure is only advisable in rare instances.

**ETIOLOGY.**—*Acute glandular* endometritis may result from trauma or taking cold during the menstrual congestion, *e.g.*, by suppression of menstruation from exposure to cold, excessive coitus, overexertion, or blows upon the lower abdomen during menstruation. Poisons, such as phosphorus and the essential oils, are occasional causes.

*Acute interstitial* endometritis is caused by infection, such as inoculation by gonorrheal pus during or following coitus, infection of retained secundines, or the extension of sepsis from vaginal inflammation. It may also follow traumatism with immediate or subsequent infection, such as lacerations of the cervix during labor or by instrumental dilatation, curettage of the endometrium, the introduction into the uterus of strong irritants, the use of intrauterine stem pessaries or poorly fitting vaginal pessaries, irritating and unclean tampons, etc.

Most gynecologists believe that when a hitherto healthy woman develops within the first year or so of married life, or after her first pregnancy, an ascending endometritis and adnexitis, the latter is surely gonorrheal in origin, though examinations of the husband have failed to demonstrate gonococci. The writer believes that in most instances there may not be a true gonococcal infection. Many of the failures of gonococcal vaccines are attributed to this fact. Other organisms may be forced into the uterus by douches given under high pressure. Moreover, in post-gonorrheal urethritis in the male, quantities of bacteria of various kinds are harbored in the urethra long after gonococci have disappeared. In some cases these organisms may cause in-

flammation of the female organs. Neisser (Med. Klin., xi, 511, 1915).

Traumatism or reinfection may convert a chronic into an acute endometritis.

*Chronic glandular* endometritis may be caused by interference with the menstrual function by taking cold, overexertion, excessive coitus, laborious or sedentary occupations, uterine displacements, obstinate constipation, etc. The same causes may act during puerperal involution or after abortion. Excessive coitus, masturbation, ovaritis, uterine fibroids, inflammation in neighboring pelvic organs, and interference with uterine drainage by stenosis may lead to it.

Acute attacks and the above-mentioned causes increase the hyperemia and evolutionary changes of the endometrium that prepare it for the formation of the decidua, and disturb the involution that normally follows each menstruation. Hence, glandular endometritis differs at first but little from a subinvolution of the endometrium, and is not an inflammation according to the ordinary acceptance of the term.

The researches of Hitschman and Adler and others showed that endometrial lesions formerly regarded as inflammatory are in reality to be considered as alterations related to menstruation. The premenstrual endometrium shows a pronounced tendency to hyperplasia, becoming three or four times thicker than normally, with the cells edematous, the glands elongated, tortuous and distended with secretion, and the mucosa as a whole simulating a decidual formation. On the basis of these findings, some authors have even denied the occurrence of chronic endometritis; a more general opinion is, however, that true inflammation of the endometrium should be regarded as present only, where there is round-cell and plasma-cell infiltration, together with indications of fibrosis.—Ed.

Fig. 3



Fig. 2



Fig. 1

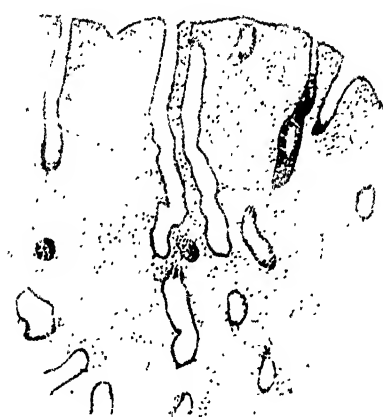


Fig. 4



Fig. 5



Comparative Histology of Endometritis. (Zweifet.)

Fig. 1, normal mucous membrane Fig. 2, beginning erosion of cervix. Fig. 3, glandular endometritis  
Fig. 4, acute and chronic interstitial endometritis. Fig. 5, chronic interstitial endometritis



*Chronic interstitial* inflammation may result from one or more acute attacks or from infection by objects introduced into the vagina or uterine cavity, whether by operation, examination, or improper attempts at medication.

**PATHOLOGY.**—The mucous membrane of the cervical cavity presents the same changes as those of other mucous membranes.

The alkaline mucous discharge that hangs from the cervix, together with the congestion and infiltration, often produces an exfoliation of the epithelium about the external os, with reproduction in the form of immature cylindrical epithelium. This condition is called *simple erosion*. The infiltration and swelling of the sub-mucous tissues cause more or less of a rolling out, or eversion, of the mucous membrane of the cervical cavity, which is more pronounced on a lacerated cervix. More or less folding of the infiltrated mucous membrane may give the appearance of a papillary or granular surface, which is called *papillary erosion*. Pockets may form in these folds, and, together with the everted cervical glands, may become occluded, giving rise to a cystic condition called *follicular erosion*. These follicles may become so numerous, or one or two may become so large, that the normal cervical tissue is either displaced or replaced by them, and *cystic degeneration* results. Sometimes localized hyperplasias are present, with projection of glandular polypoid masses.

Some of the above-mentioned changes are shown in the annexed colored plate.

The uterine mucous membrane above the internal os has somewhat different characteristics from those

of other mucous membranes which have different functions. Its glands are simple depressions or epithelial tubules that extend to the muscular walls underneath. Instead of being imbedded in firm connective tissue as are the cervical glands, they are surrounded at their inferior extremities by muscular fibers projecting from the muscular walls, which constitute an ill-defined muscular structure called the *muscularis mucosæ*. In the interglandular or intertubular spaces or fluid are found delicate connective-tissue fibers and round or oblong cells resembling lymph-cells.

Following the investigations of Hitschman and Adler, showing that many so-called cases of chronic endometritis were attended merely by physiologic changes due to the menstrual function, it became a fairly general opinion that chronic endometritis was a comparatively infrequent condition. This opinion is questioned by the writers on the basis of 2½ years' examination of routine curettings. They believe that, to make a diagnosis of chronic endometritis, it is necessary to find small round cells; if alone, in considerable quantity. These must infiltrate the upper half of the endometrium either in a diffuse manner or in small groups. They should also be found, if present in any great number, grouped around the glands, both superficial and deep. In 305 specimens, they were able to diagnose chronic interstitial endometritis in 70 cases. These are divided into classes according to the menstrual phase. This placed 16 specimens in the early premenstrual phase; 1 in the menstrual phase, while postmenstrual mucosæ were found 15 times, 7 early and 8 late. Thirty-seven specimens were found in the interval. The glands were pathological in 12 instances, the diagnosis of gland hypertrophy being made 5 times and of

gland hyperplasia 7 times. There was one senile endometrium, and in 2 cases there was tuberculosis. Small round cells were found alone 24 times, with plasma cells 41 times, and with polynuclear leukocytes 5 times. Chronic interstitial endometritis is rather frequently met with. The presence of small round cells alone in marked numbers, as was the case in 24 instances in the writers' series, is sufficient evidence for a diagnosis of chronic interstitial endometritis. Schwartz and Kohlbray (Jour. Mo. State Med. Assoc., xvi, 209, 1919).

When subjected to intense, prolonged congestion, an infiltration of serum takes place, raising the epithelial surface and causing a proliferation of the epithelial cells, with enlargement, as well as wrinkling, twisting, or bending of the glandular tubules, or, in severe cases, a formation of new depressions or tubules, some of which may become closed by bending or swelling at their orifices.

In some cases the epithelium proliferates within the glands, forming more than one layer. Round-cell infiltration and formation of new interglandular tissue may take place, with proliferation of the epithelial cells within the glands so that they may form more than one layer, particularly if septic infection intervenes. In such cases agglomerations of glands surrounded by a small amount of connective tissue project from the surface, forming polypoid masses, which may spring from every part of the mucous surface.

The uterine walls are usually also congested, and some round-cell infiltration takes place about the blood-vessels, which, in time, leads to the formation of adult connective tissue. Contraction in this connective tissue may finally cause anemia of the uter-

ine walls and more or less atrophy of the muscular fibers.

The mucous membrane is hyperemic, softened, thickened, and dark red in color. In places it may have a mottled appearance, due to minute extravasations of blood. The surface is smooth, sometimes irregular, and is moistened with a thin, clear, grayish or pinkish mucus. The pouting mouths of the congested and enlarged glands are visible. The uterine walls are slightly thicker and the uterine cavity somewhat longer than normal (from  $2\frac{1}{2}$  to 3 inches deep from the external os to the fundus). This condition is that of *glandular* endometritis, or *hyperplasia* of the endometrium, and is seldom the result of infection. It is, as a rule, chronic.

Hyperplasia of the endometrium, as first described by Cullen in 1900, is one of the most important of all endometrial lesions. Its characteristic symptom is bleeding. Pathologically it exhibits hyperplasia of both epithelial and stromal elements in varying degree and proportion. In sections the glands are of the "Swiss cheese" pattern, large dilated glands occurring side by side with small and narrow glands. The epithelium may be considerably thickened, while the stroma is often over-abundant and may show mitoses. Grossly the endometrium may be enormously increased in amount, and may present the picture often incorrectly described as "chronic polypoid endometritis." In nearly  $\frac{1}{2}$  of the writers' 66 cases, however, it was of normal thickness, and in over  $\frac{1}{2}$  it was smooth. The hyperplasia may be localized in uterine polypi, in which case bleeding is usually absent. About  $\frac{1}{2}$  the cases were over 40 years of age. No definite abnormality in menstrual history prior to onset of the symptoms of hyperplasia was noted. At such onset there was nearly always excessive

menstruation, usually both as to amount and duration. Passage of clots is not unusual. Amenorrhea occurred in  $\frac{1}{6}$  of the cases. Pregnancy occurred in but 2 cases after onset of hyperplasia, although about  $\frac{1}{2}$  of the patients had previously had full term pregnancies. The most important and largest group of hyperplasia cases is that occurring at or near the menopausal age; these cases come into diagnostic conflict with cancer. In many instances climacteric bleeding proves to be due to hyperplasia, a benign condition with no tendency toward malignancy. E. Novak and Martzloff (*Amer. Jour. of Obstet. and Gyn.*, Oct., 1924).

During the menstrual periods the congestion is intense, and there is more or less extravasation of blood in the interglandular spaces, leading to extensive exfoliation of the epithelium and detachment of mucosa.

When the congestion results suddenly from causes acting during or just before the menstrual period, it is also intense and accompanied by interglandular extravasation and blood-stasis that interfere with the menstrual discharge, and which, if not relieved, run into the chronic form.

In *acute septic* endometritis the blood-vessels of the endometrium are engorged and increased in number. There is considerable exfoliation and proliferation of the epithelial cells, sometimes to such an extent as to cause a superficial necrosis. The interglandular spaces are crowded with round cells, leucocytes, and cocci, which may extend into the muscularis mucosæ, and, if streptococci be present, a short distance into the uterine walls. Congestion, extravasation of blood, serous and round-celled infiltration take place throughout the uterine tissue, and a fibrinous exudate may appear on the peritoneal surface.

There is a more or less abundant flow of pus from the endometrium.

Investigation on puerperal endometritis which led to the conclusion that the antecedents and modern obstetric procedures are apparently not causative of this condition, which, on the other hand, seems to bear a close relation to constipation. The writer urges more dependence upon the bactericidal power of the lochia. Flushing of the uterus or vagina is thus contraindicated, as it removes the antibodies furnished by the system before they have had an opportunity to carry out their curative function. Indicated measures are **vaccine therapy, heart tonics**, and procedures tending to **enhance leukocytosis**. The causative infection in the author's cases was found to be either a pneumococcus or *Streptococcus viridans*. Gret (*Semana méd.*, Aug. 10, 1922).

In *chronic septic* endometritis round cells and leucocytes crowd the interglandular spaces, compressing the glands, and in places penetrating and destroying them. After a time, the formation of contracting adult connective tissue compresses and obliterates some glands, and obstructs the mouths of others, converting them into small cysts. The epithelium in the atrophic glands and on the surface also degenerates, so that in old and senile cases the mucous membrane may be represented by a thin layer of sclerotic connective tissue with only vestiges of epithelial structure.

The uterine walls, at first hyperemic and infiltrated to a greater or less depth with serum and round cells, are thicker and softer than normal, but later, owing to the contraction of the inflammatory tissue, become hardened. The atrophy of the muscular tissue and absorption of the serum, as well as the senile changes, may

finally lead to a diminution in size of the entire organ.

Endometritis occurring in connection with absorption may interfere with the atrophy of the decidua, and masses of decidual cells may be found in the endometrium in connection with the round-cell infiltration.

In cases of hyperplasia of the uterine mucosa in mature women the author has sometimes found inclusions in this mucosa which exhibited the morphologic appearance of remnants of gestation products. Post-abortion endometritis seems to be the cause not only of metrorrhagia but also of the frequent endometrial hyperplasia following interruption of a pregnancy. Such endometritis may likewise hinder maturation of the ovarian follicles, the stimulus connecting the ovarian with the uterine functions travelling, under these circumstances, not from the ovary to the uterine mucous membrane, but in the reverse direction. Lahm (Zent. f. Gyn., Aug. 14, 1920).

In some cases the menstrual congestion is so great that an acute attack is practically lighted up at each period. The stroma-cells are enlarged and resemble decidual cells, and the tissues are crowded with leucocytes. The congestion is so great that there is an abundant extravasation of blood in the interglandular spaces, which so loosens the superficial portion as to cause its exfoliation in places or even entire, as a more or less complete cast of the uterine cavity.

After the menopause the cervix may become stenotic, and the discharges be retained. The uterine cavity may then become distended by an offensive and purulent fluid, and the uterine walls attenuated.

The term **chronic endocervicitis** has been used by Sturmdorf as a comprehensive appellation covering such various manifes-

tations as cervical catarrh, simple follicular or papillary erosion, eversion, ectropium, ulceration, hypertrophy of the cervix, etc., all of which are held to depict merely different features of the same infectious process. He regards the cervix as an important focal source of infection, from which, through a chronic ascending lymphangitis—and not an endometritis, the corporeal endometrium being rather resistant to infection—there may result impairment of uterine, tubal, and ovarian functions, and in particular, disturbances of menstruation, fecundation, and decidualation.

Infection of the cervix, according to Sturmdorf, may date back to a vulvitis in early infancy. By far the commonest provocative organism in chronic endocervicitis is the gonococcus, streptococcus, staphylococcus and colon bacillus infections following it in order. Predisposing to it in infants are the exanthemata, protracted diarrheas, and general debility; in adults, cervical maldevelopment and trauma by cauterizations, dilatations, curettage, or birth injuries. Objectively, in the nullipara with dysmenorrhea and sterility there is an inflammatory halo encircling a small pouting os with a tenacious clump of mucus; in the multipara, there are lacerated, eroded hypertrophied lips, honeycombed with Nabothian cysts under a granular surface that bleeds at the slightest touch. The condition is primarily an infection of the deeply situated terminal tufts of the endocervical muciparous glands. The cysts result from duct occlusions, while if the process becomes purulent, the cervix is riddled with chronic miliary abscesses.—Ed.

**PROGNOSIS.**—The prognosis of acute interstitial metritis in the puerperal state or after abortion is grave. The patient may die of septicemia, or the disease may extend to the Fallopian tubes, ovaries, and peritoneum, or into the veins or lymphatics of the broad ligament, or may lead to chronic endometritis and subinvolution.

When not connected with pregnancy the disease seldom terminates fatally, but is apt to extend to the adnexa or become chronic.



**Acute cervical metritis** may end in recovery, but usually becomes chronic.

**Chronic cervical metritis** may get well, but, as a rule, it persists for a long time. It can ordinarily be cured by local treatment or operation.

**Chronic corporeal endometritis** of the septic variety is apt to get well if there is good drainage through the cervix. Without adequate drainage it becomes chronic and is liable to spread to the adnexa.

In cases of long standing the septic condition can be removed, but the endometrium and myometrium can seldom be restored to a normal state.

The sterility is apt to be permanent.

**Chronic glandular endometritis** can generally be cured by treatment. Mild or recent cases may get well spontaneously, but severe cases usually persist for a long time, or until the menopause.

**TREATMENT.**—Where suppression of the menses results in the condition that has been termed *acute glandular metritis*, the flow should be re-established, if possible, in the early or congestive stage. As soon as possible after the suppression the patient should take a **warm sitz-bath** (100° F.—37.8° C.) and go to bed. **Hot drinks, hot applications to the abdomen and groins, and hot-water bags or bottles to the feet and legs** should be employed. In married women **scarification of the cervix** may be used with benefit. The production of slight nausea by means of **tartar emetic, ipecac, or lobelia** is useful as a sedative to the congested pelvic organs. If the menstrual flow is re-established by these means within a day or two, the patient may leave the bed after the flow has ceased, but should lie down two or three hours in

the middle of each day, and take but little exercise for three or four weeks. At the time of the next period she should keep to the bed and repeat the hot applications, etc., if the flow does not appear on time. The bowels should be kept open by **salines**.

If the menses are not re-established within two or three days after their suppression, the patient should remain in bed for a week or ten days, apply **counterirritants** over the iliac and suprapubic regions, and take copious **hot douches** (115° to 120° F.—46.1° to 48.9° C.) two or three times daily in the recumbent posture. She should secure a daily evacuation of the bowels, and, if practicable, introduce small cotton **tampons**, saturated with a 10 per cent. solution of **ichthyol** in boiled **glycerin**, high up in the vagina every other day, and leave them for about eighteen hours. **Tonics** and an easily digested **diet** should be prescribed.

*Acute septic metritis* following labor or abortion calls for a thorough **evacuation of the uterus by the fingers or dull curette**, and, if septic symptoms persist, antiseptic **intra-uterine douches** every twelve hours (1:3000 **mercuric chloride** followed by sterile water or 1 per cent. **creolin**) and **vaginal douches** of the same character every six or eight hours.

The efficiency of **turpentine** in puerperal endometritis has been emphasized by Gutierrez. A wick of gauze impregnated with it is introduced into the uterus, and induces such profuse exudation that any retained scraps are washed out. The uterus is, however, previously flushed with sterile water.

In the acute puerperal endometritis and metritis attending *sapremia*, i.e., dependent upon decomposition-infection of retained membrane, placenta, or blood clot, Bland counsels against the giving of douches. If

the cervical canal is found widely dilated, the necrotic mass may be removed manually or by instrumental means under anesthesia. This is to be followed by free **uterine irrigation with hot saline solution** and the insertion of an **iodoform gauze tampon**. If, however, the cervical canal is contracted, it is well to wait for subsidence of the acute symptoms, then **dilate** the uterine cavity and withdraw the contents manually or instrumentally, and finally **irrigate the cavity and pack with iodoform gauze**. Curettement may do more harm than good in these cases.—Eh.

When the attack follows an operation, an **ice-bag** should be kept on the lower abdomen for twenty-four or thirty-six hours, the infected surfaces disinfected by a strong antiseptic, and one of the above-mentioned antiseptic **douches** used either to the endometrium or vagina as required.

As the inflammation subsides, **hot douches, laxatives, tonics, rest in bed, etc.,** are indicated.

In *chronic* uterine inflammation all causes of the disease and all conditions that perpetuate it should receive attention.

Displacements should as far as possible be corrected, stenosis relieved, and pelvic inflammatory conditions and tumors treated or removed.

The patient should remain in bed during a portion or all of the menstrual period, and take more than ordinary care of herself after abortions or confinements.

Chronic glandular endometritis, alone or with chronic septic or interstitial endometritis, and all menorrhagic cases uncomplicated by pelvic peritonitis, should be **curetted**.

When the **curette** is employed due care should be exercised. Rough manipulation and undue pressure upon the uterine surfaces have been followed by untoward results.

Exfoliative endometritis and polypoid endometritis may require more than one **curettage**.

In a large proportion of cases the cervical canal is small or bent, and must be kept **dilated** for several weeks to promote uterine drainage.

In others it is necessary to use strong **astringents** and **antiseptics** to the endometrium, for the purpose of counteracting the tendency to a recurrence of the hyperplasia or sepsis.

The **hot vaginal douche** twice daily acts beneficially as a sedative to the pelvic circulation, and aids in keeping the vagina clean.

Local treatment may be commenced in two or three weeks after the operation. If the cervix is small or bent, a round **dilator**, or male **urethral sound** No. 12 to No. 15, should be passed through the internal os once or twice a week. In order to avoid infection, the patient should take a large, **hot vaginal douche** shortly before treatment, and the gynecologist should wipe out and disinfect the vaginal fornices and cervix through the speculum before introducing the disinfected sound.

After the sound is withdrawn a 50 per cent. solution of **ichthyol** in glycerin may be applied to the endometrium, or, if the case has been a hemorrhagic one, pure **lysol** or **phenol**, or a 20 per cent. solution of **zinc chloride**, every ten days to two weeks.

Good results with **magnesium sulphate** have been reported by C. J. Wallace. An ounce of the remedy in crystals is poured into the vagina and confined there until, by osmosis, it causes a free discharge from the pelvic tissues. This, if repeated daily for one week, will reduce a large, spongy uterus to normal dimensions.

**Hot vaginal irrigations** are extremely valuable. Two or 3 gallons

(8 to 12 liters) of solution at 105 or 110° F. (40.6 or 43.3° C.) should be used morning and evening, and **depleting tampons** should be introduced 2 or 3 times weekly. These not only hygroscopically relieve the engorgement, but, by maintaining the uterus high in the pelvis, improve the uterine circulation also. If the cervical canal is patulous and drainage is free, **intra-uterine applications** may be made. Ordinary **tincture of iodine** is probably most valuable; **argyrol**, 25 per cent., or **silver nitrate**, 5 per cent., may be employed. If simple medical measures fail, **dilatation** and **curettement** may be practised, followed by **cauterization** of the interior with **tincture of iodine** and the introduction of an **iodoform gauze drain**. Radical operation is rarely indicated, and should be performed only after all other measures fail. P. B. Bland ("Gynecology," ii, 750, 1925).

When there is a tenderness or irritation in the tissues beside the uterus, curettage and intra-uterine medication are liable to do more harm than good.

In such cases a copious **hot vaginal douche** (120° F.—48.9° C.) should be taken at or near the noon hour, followed immediately by two hours of **rest** in the recumbent position and another douche at bedtime, followed by the introduction into the vaginal vault of a **tampon** saturated with a 10 per cent. solution of **ichthyol** in **glycerin**. The tampon is removed when the noonday douche is taken.

**Laxatives, tonics, massage, regulated out-of-door exercise, and restriction of coitus** are useful adjuvants.

Endometritis with stenosis and pyometra (so-called *senile endometritis*) should be treated on the same principles as any pus cavity, *viz.*, **dilatation of the cervix** for drainage, and washing out of the uterus with **antiseptic solutions** once or twice daily.

*Chronic cervical endometritis* should be treated by local applications made through the vaginal speculum. Simple and papillary erosions yield quickest to astringent and stimulating remedies, such as **phenol**, **creosote**, and strong solutions of **chloride** or **persulphate of iron**. Follicular cervicitis yields quickest to iodine applications. A mixture of 2 parts each of **iodine** crystals and 95 per cent. **phenol**, and 1 part of **glycerin**, is efficacious, and should be applied twice weekly. Retention cysts should be punctured before the application is made. Antiseptic and astringent douches, such as a 1:1000 solution of **potassium permanganate** or of **zinc chloride**, may be employed with benefit twice daily.

Where there is moderate cyst formation or cystic degeneration in a limited area, or as an alternative to trachelorrhaphy or trachelotomy when such operations are not available or advisable, the efficiency of local treatment is increased by the use of **multiple scarification**. The scarificator I employ is bayonet-pointed and cuts in three directions, thus leaving openings for the escape of mucus and penetration of a solution simultaneously used, *viz.*, 1 part each of **iodine** crystals and **glycerin** and 2 parts of **phenol**. From fifty to a hundred punctures into the diseased area or areas are made at short intervals—once to twice a week. The procedure is simple and can be carried out at the office. The vaginal fornices, cervix, and cervical cavity are first wiped dry with absorbent cotton and disinfected with 5 per cent. **phenol** solution. Five or six punctures into and about each retention cyst that can be seen or felt are then made, and also

into any red spots or areas. Cotton is next pressed firmly against the surface to express mucous plugs and stop oozing. Then, with an applicator tipped with non-absorbent cotton, the solution is applied freely and with pressure to the scarified areas and the mucosa both of the vaginal portion and cervical cavity. Finally, a dry tampon is placed against the cervix, to be removed by the patient in a few hours. Sometimes the treatment is begun by dilating the cervix slightly with a large sound. The treatment is repeated every three or four days until no cysts can be seen or felt. Thereafter, once a week for three or four months, fifty to a hundred or more punctures are made, followed by iodized phenol. After all signs of inflammation and cyst formation have disappeared, the patient is discharged, with directions to return after three or four months, when a few more treatments for glands previously not in evidence may be required.

Among the measures recommended for *acute endocervicitis* are vaginal douches of hot diluted **Lugol's solution** 3 times a day; applications of pure **tincture of iodine** on alternate days or 25 per cent. **argyrol** solution daily to the cervical canal and vaginal portion of the cervix; later, a **tampon** of 10 per cent. **ichthyol** in **glycerin**, and applications of 10 per cent. **silver nitrate** solution in the cervical canal every 2 or 3 days.

In *chronic endocervicitis*, applications of 10 per cent. **silver nitrate** solution as far as the internal os, preceded by swabbing of the cervical canal and lips with cotton saturated with **sodium bicarbonate** solution, are advocated by Bland. The silver solution is allowed to remain for 5 minutes, and the procedure repeated on alternate days. **Radium** has proven effective in these cases, but must be used only with great caution in women of child-bearing age.

While **surgical treatment** for chronic endocervicitis has generally been considered

indicated only where medical measures fail or there is cervical laceration definitely calling for operation, Sturmdorf, impressed with the importance of the cervix as a focus of infection and the difficulty of curing infection in the deeply situated racemose glands of this structure, has particularly stressed the value of operation, and devised a special procedure for these cases.

In **Sturmdorf's operation**, the diseased endocervix is completely removed, but very little of the cervical muscle, so that less scar tissue follows than after the earlier classical operations on the cervix. By a circular incision an ample cuff of mucosa is first formed from the vaginal covering of the cervix. The endocervix is next excised from the surrounding muscle-bed as a cone-shaped mass with its apex at the internal os and its base formed by the everted external os. Suitable sutures are then inserted to draw the cuff of mucosa into and make it reline the resulting cone-shaped cavity: Long strands of No. 1 chromic catgut are passed through the free borders of the anterior and posterior mucosal flaps in the form of mattress-like sutures. These sutures are then carried into the cervical canal just above the internal os and passed through the cervical wall so as to emerge on the vaginal surface at the bases of the corresponding flaps. When these sutures are tightened and tied, the cavity becomes lined with the cuff of mucosa. If the edges of the flaps are not thus accurately brought together, some superficial sutures may be added.—Ed.

In *gonorrheal cervicitis* and *endometritis* the following treatment is indicated. *Acute cases*: 1. Confinement to bed. 2. Keep emunctories active. 3. Limit diet. 4. Cleanse vagina frequently with large amounts of hot **saline solution** or **hot water** containing **boric acid** or a weak **iodine** solution. Use irrigator with nozzle projecting a straight forcible stream, and pinch mucous membrane of introitus around nozzle, to flush cavity satisfactorily. Intra-uterine measures and pelvic operative intervention contraindicated. *Sub-acute cases*: 1. Soften and dilate cervix with Goelet's uterine **electrodes** and **galvanic current**. 2. Flush uterine

cavity with hot **iodine solution**, 1 dram (4 c.c.) of the tincture to a quart of water, or **silver nitrate**, 1:5000. 3. As condition improves, substitute daily intra-uterine injections of **iodized phenol** (equal parts of iodine tincture and phenol) or 1 per cent. **silver nitrate**. Use syringe with long pliable nozzle, with its tip wrapped with cotton; inject fluid into cotton and withdraw syringe. Insert **iodine-glycerin tampon** (1 dram to 4 ounces), which patient is to remove next morning. Remove cotton within uterus at next visit. Dannreuther (Med. Record, Nov. 4, 1921).

About 10 weeks after delivery there is often found a slight or moderate cervical laceration with mild endocervicitis. If unrelieved, this leads to inflammatory changes, cystic degeneration, a vicious circle of symptoms, and finally an operation with only partially satisfactory results. In these patients the writer uses a small **electrocautery**, with which, in the average case, he burns down the excessive granulations resulting from the eversion, healing then taking place. If there is more than average trauma, 3 or 4 linear incisions are made on both the everted lips. Application of 4 per cent. **cocaine** solution and insertion of a small tampon of the same solution into the cervical canal for a few minutes yield sufficient anesthesia for this procedure. If the vaginal surface of the cervix can be avoided, no anesthesia is needed. After a second treatment in 2 weeks, and the lapse of 6 weeks more, the condition is usually normal except for the lacerations, which are not pathologic in themselves.

Subinvolution is always markedly benefited by this treatment. In cases requiring a more extensive destruction of glandular elements, the patient is anesthetized at the hospital and a larger cautery used. This method has markedly reduced the number of plastic operations performed. Hilliard E. Miller (Amer. Jour. of Obst. and Gyn., Jan., 1925).

In the *chronic* form in the *upper cervix* or *near the os*, the treatment calls, first of all, for **dilatation**. Stimulating applications before dilatation are not always well borne and sometimes aggravate the condition. Gradual progressive dilatation is preferred to extreme divulsion at one sitting. The repeated mild stimulation of progressive dilatation with **graded round dilators** not only causes a steady improvement, but often cures the sterility, due mainly to exudate.

Before the dilatation the vaginal vault and cervix are swabbed thoroughly with a 5 per cent. solution of **phenol** followed by a 20 per cent. solution of **phenol in glycerin** to the entire uterine cavity. When a round dilator equal in size to a No. 25 urethral dilator (French scale) can be passed without causing a show of blood or producing much pain, a stimulating solution of **iodized phenol** is applied to the entire cervical cavity and dilatation is done twice a month for a few times and then once a month until the parts are in fairly normal condition. When the lumen is large the same treatment is used except that it is begun and ended with large dilators.

HENRY T. BYFORD,  
Chicago.

### ENURESIS.—DEFINITION.—

An involuntary discharge of urine or incontinence of urine which may be due to many different conditions.

**SYMPTOMS.**—If we may speak of the symptomatology of this affection, which in itself, in the majority of instances, is to be regarded as a symptom rather than as the actual disease, the ground is amply covered by the single statement which

is usually detailed by the parent or the patient, that there is an involuntary passage of urine.

It is not very difficult to discover the presence of enuresis, but the determination of the cause or the causes for its existence is by no means so easy and is sometimes rendered impossible. Enuresis is not liable to be mistaken for any other affection, with the single exception of the incontinence, or overflow, symptomatic of retention of urine due to prostatic enlargement or some other obstruction to the genitourinary tract, from the bladder outward.

**ETIOLOGY.**—Incomplete development of the sphincter muscles, existing in the infantile period, may persist for an abnormal time (beyond the second year); when this occurs, it is followed by the involuntary emission of urine. This may be due to insufficiency of the sphincter vesicæ muscle, which allows the urine to enter into the upper part of the urethra; it is expelled by a reflex action of the detrusor urinæ muscle.

Enuresis may also be caused by debility of the neck of the bladder and of the internal sphincter, or through its inadequate control from disease of the spinal cord and of the nerve-centers; and also through overdistention of the bladder.

Case of enuresis in an elderly man in whom posterior urethroscopy revealed a large and anesthetic colliculus seminalis, possibly a forerunner of tabes. The condition of the verumontanum returned to approximately normal after potassium iodide treatment. I. Deutsch (Zeit. f. Urol., 20, 1, 1926).

In a number of cases enuresis may be a local manifestation of a general lack of tone of the entire muscular system. Many cases suffer from

marked nutritive disturbances attributed to reflex causes alone. Even where there are no gross evidences of malnutrition, the metabolic activity in the sensitive nerve-cell is probably disturbed.

In cases of hypothyroidia the impaired oxidation due to inadequate activity of the thyroid entails reduced muscular power, including that of the sphincter muscles, as emphasized by Hertoghe, Sajous and others.

Enuresis is a local spasm due to hypervagotonia of the pelvic plexus. The writer has observed cases in which the incontinence disappeared when asthma, eczema or an infectious disease appeared, or *vice versa*. Five drops of a solution of 0.01 Gm. ( $\frac{1}{10}$  grain of **atropine sulphate** in 10 Gm. ( $2\frac{1}{2}$  drams) of water, before retiring, is advised for children between 4 and 10. The dose should be increased every 2 days, up to 10 or 20 drops. The remarkable efficacy of this treatment the author deems convincing proof of the excessive irritability of the vagus innervation of the bladder. Subcutaneous injections of **adrenalin** and **pituitary** extracts gave good results in 2 adolescents with enuresis. Organotherapy, especially **thyroid extract**, may be efficient. In cases of enuresis with changes in the urinary acidity, **phosphates** and **sodium bicarbonate** are successfully used. Epidural injection of **iodized oil** is a helpful adjuvant in the treatment. Sicard (Annales de Méd., May, 1925).

Diseases of the nervous system, both functional and organic, are recognized as factors in producing this disease. According to Rachford, incontinence of urine in children is a true neurosis and not, as a rule, due to muscular incompetency of the sphincter vesicæ. It rests upon excitability of the nerve-centers produced by heredity and age; anemia with consequent malnutrition, in-

creasing the excitability of the nerve-centers, and reflex irritation. Anesthesia of the bladder has been noted in a large proportion of cases by Ozerezkowski.

Heredity is a potent predisposing factor in many cases. *Monro* reported, as an example, a family in which the 6 children inherited the disorder from their father. The 2 elder children, girls, are always more affected toward the menstrual period. The incontinence affected most all of the children alike by day and night. Two of the children were subject to fits, which began during early childhood, and they also showed other signs of degeneracy. Enuresis is frequently associated with epilepsy and with affections of the spinal cord, especially *spina bifida occulta*.

Enuresis, both in children and adults, not necessarily merely nocturnal, may occasionally be a sign of *spina bifida occulta*, and may exist without other signs. Examination of the sacrum and lower lumbar vertebrae by X-rays is diagnostic. *Spiller* (*Amer. Jour. Med. Sci.*, Apr., 1916).

The cause of frequent urination in girls and women in 1000 cases was traced to concomitant complications of the sexual and child-bearing functions; in the earlier age periods acute infections were the main factors when these affected the urethra or trigone. Post-operative catheterization was a relatively common cause of frequent micturition. *H. G. Bugbee* (*Jour. Amer. Med. Assoc.*, Mar. 3, 1917).

As to the local conditions which produce incontinence, there may be mentioned overdilatation of the bladder with urine; hyperacidity of the urine; cystitis; phimosis, or an adherent prepuce, either of the glans penis or of the clitoris; nephritis; pyelitis; vesical and renal calculus; glycosuria, and rectal irritation.

The writer observed 2 cases of nocturnal incontinence occurring as an early symptom of renal tuberculosis. In 2 other cases incontinence appeared after nephrectomy. *Constantesco* (*Jour. d'urologie*, May, 1912).

Contraction of the bladder may cause incontinence. *Robson* reported the case of a single woman, aged 30, in whom bimanual examination revealed that there was practically no bladder, it being merely represented by a small, hard lump about the size of a walnut.

Masturbation has been regarded as a prolific cause of enuresis; but the frequency of this habit in children would tend to suggest that the two disorders may occur coincidentally rather than that there exists a causal relationship between them. In girls friction of the clitoris is a local irritation which, acting reflexly as does phimosis on this organ, might cause enuresis.

A study of about 200 cases in children between 4 and 12 years of age indicated that enuresis is never a disease entity, but a symptom of an underlying general neuromuscular fatigue. The fatigue is chronic and the patients are all of the overactive, nervous type. There is often an element of marked mental strain from too prolonged school work. The treatment is exclusively dietetic and hygienic. *J. I. Grover* (*Jour. Amer. Med. Assoc.*, Aug. 24, 1918).

Children are liable to fissure of the anus with far greater frequency than is generally believed, and this may excite involuntary urination. Constipation and the presence of worms (mostly *ascarides*) are among the more common causes of this disease.

With regard to causation, enuresis may be roughly divided into 5 groups: (1) Genitourinary, (2) nervous, (3) malformations, (4) general, and (5)

idiopathic. As regards the first the urine may be at fault; there may be hyperacidity or excessive alkalinity, or there may be bacteriuria. Inflammation of various parts of the genito-urinary tract, calculi, new growths, etc., may be responsible for the disorder. The nervous causes are very numerous and many are reflex in character, such as balanitis, vulvovaginitis, worms, etc. Malformations of the spinal cord or of the genito-urinary organs may be accompanied by it. As general causes may be mentioned rheumatism, thyroid insufficiency, diabetes, etc. Still found enuresis associated with rheumatism in about 5 per cent. of his cases. J. Allan (Prescriber, Aug., 1912).

A strict differentiation between polyuria and incontinence of urine and pollakiuria, or excessive frequency of micturition, is very important. Observations on 1500 cases showed that in a great percentage of cases pollakiuria is a neurosis, brought about by malfunction of a distant organ, especially eyestrain. A systematic inquiry as to frequency of micturition in refraction cases under the author's observation showed that of 1500 cases, 316 (140 men and 176 women) suffered from pollakiuria. In this series the percentage of recoveries in women was twice as large as in men. W. W. Kahn (Jour. Amer. Med. Assoc., Dec. 7, 1918).

Enuresis may follow labor, owing mainly to the traumatism, pressure, etc., to which the bladder, the glands, and the urethra are subjected during the process.

**PROGNOSIS.**—When the cause can be discovered and removed, the prognosis is favorable; in elderly people, however, the affection is generally due to paralysis or deep-seated disease of the urinary organs. The outlook is usually favorable in cases of enuresis nocturna. Sometimes, however, it proves to be a very obstinate malady.

**TREATMENT.**—The cause of the disorder should be discovered and its removal effected.

Atonic conditions, in children as well as in adults, often lie at the foundation of the lack of control over the passage of urine, and, in these cases, **outdoor exercise** should be advised and a carefully selected diet prescribed for its nutritiousness and digestibility. A vegetable diet has been advocated.

A **vegetable diet** is the ideal one for children with enuresis nocturna. **Restriction of fluid intake**, including milk after 4 P.M., **raising the foot of the bed**, making the child sleep on its side, and systematic **waking up** of the child to have it **urinate regularly**, are helpful. Most children addicted to enuresis are exceptionally hard sleepers and are not aroused by the desire to urinate. This can be remedied by having the child take a **nap** for two hours, **morning and afternoon**. Klotz (Deut. med. Woch., Dec. 5, 1912).

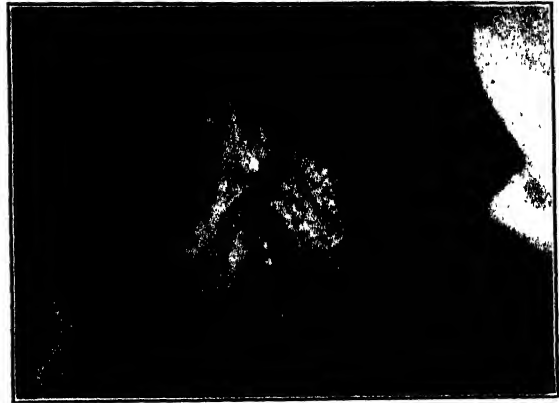
Whether diurnal or nocturnal, or both, the writer has obtained the best results by anticipating the involuntary act by a **voluntary emptying of the bladder**. When carried out systematically, this can preclude the use of drugs. Newlin (Arch. of Pediat., Oct., 1914).

The X-ray to determine possible presence of spina bifida, urinalysis to ascertain acidity of urine, and personal and family antecedents, are important in diagnosis. A stricture may act as cause. **Belladonna** or **atropine**, epidural injections of normal **saline solution** with **cocaine** or **lipiodol**, and **electricity**, are potent remedial resources. Bazy (Medical Press, May 5, 1926).

Of material aid are ferruginous preparations where any degree of anemia exists. The syrup of the **iodide of iron** is readily taken by children. For adults, the **peptomangan** (Gude) is a serviceable tonic. The dose of the first is from 3 drops upward, well



Mrs. S., aged 22 years.



Gladys D., aged 4 years.

Elizabeth W. aged 5 years



Phimosia as a cause of enuresis in the female. (*McGirk.*)

diluted with water; and of the second a dessertspoonful to a tablespoonful, in milk or wine. Jacobi spoke highly of the **elixir pepsini, bismuthi et strychninæ** of the National Formulary in insufficient gastric digestion associated with atony of the stomach a child of 3 years taking a teaspoonful three times a day.

The writer advocates **outdoor life**, avoiding excitement and fatigue. **Diet** chiefly of vegetables; no heavy meals; no fluid at the evening meal. **Tepid shower baths** morning and evening with a **dry rub**; in refractory cases, **cold wet packs**. **Atropine sulphate** in 0.1 per cent. solution, 5 drops at bedtime, increased by 1 drop each night up to 10 or 12 drops; if there is also *diurnal* incontinence, 1 drop 3 times a day is added. If this fails, Zuber's solution of **phosphoric acid** (50 per cent.), 17 Gm., and **sodium phosphate**, 34 Gm., in water, 250 c.c.; 1 or 2 teaspoonfuls 3 times daily with the meals. Comby (Bull. Soc. méd. des hôp. de Paris, Mar. 13, 1924).

The writer reports 2 cases successfully treated with **madder**. It is given in a decoction, 3 tablespoonfuls to 3 cupfuls at a dose, or as madder flour in jam or an electuary. As much as 10 Gm. (2½ drams) causes no untoward effects. In children 6 Gm. (1½ drams) may be incorporated with 150 Gm. (5 ounces) of wheat flour to make 12 zwiebacks. A. Bauer (Zeit. f. Urol., xviii, 452, 1924).

Incontinence due to a weakness of the sphincter muscle is best relieved by ascending doses of **strychnine** or the tincture of **nux vomica**. In appropriate cases, strychnine is a very efficient agent.

**Douching of the perineum with cold water** has been advised by some writers as a very useful measure. It is not a disagreeable procedure if care is taken to concentrate the douche on the genitoanal region.

In both diurnal and nocturnal enuresis in children the sudden **cold douche** to the anal and **perineal region** is very effective. It may be done on a special chair with open seat. Klotz (Berl. klin. Woch., May 1, 1911).

The **faradic current**, one electrode being placed in the rectum and the other over the perineum in the male and the mons veneris in the opposite sex, has been advocated. The current is to be gradually increased. Or, as advised by Cipriati, a sound, the end of which forms an electrode, is introduced into the urethra as far as the sphincter of the bladder, and its free end is attached by a chain to one of the Leyden jars; the machine is regulated to give 6 to 8 sparks a second, and each sitting lasts five minutes.

If incontinence is due to hyperesthesia of the mucous membrane or irritability of the bladder, the remedy indicated is **belladonna**. Baruch, Watson, and other observers bear testimony to the efficiency of this drug in the treatment of the nocturnal form of incontinence. Both belladonna and atropine are tolerated in much larger doses by children, in proportion to their size or age, than by adults. In many cases a single evening dose of the extract of **belladonna** (gr. ¼ to ¾ to 1—0.016 to 0.048 to 0.065 Gm.) or of the **sulphate of atropine** (gr. 1/100 to 1/75—0.0006 to 0.0008 Gm.) answers sometimes to an unexpected degree, according to Jacobi. In most cases, however, belladonna or its alkaloid must be pushed to the extreme limit before an impression is made upon the disease.

Two varieties of the complaint have to be recognized: (a) the atonic variety, and (b) that characterized by vesical irritability. In the latter antispas-

modics are especially useful, and among these **belladonna** comes first. The general consensus is that this drug must be given in large doses and pushed until signs of intolerance, such as dryness of the mouth, mydriasis, disturbances of vision, etc., are just in evidence. For a child over 5 years of age 10 minims (0.6 c.c.) of tincture of belladonna may be given thrice daily; this dose is increased by  $2\frac{1}{2}$  minims (0.15 c.c.) every few days until the full physiological effects of the drug are apparent. J. Allan (Prescriber, Aug., 1912).

In cases in which the urine is normal the treatment consists in improving the general condition of the child. Then **belladonna** should be given, beginning with 10 minims (0.6 c.c.) of the tincture two or three times a day, gradually increasing the doses up to 20 to 25 minims. The writer has never given larger doses, but he has used sometimes rather large doses of **atropine**. Even with the smaller doses of belladonna the child may complain of difficulty in seeing, dry mouth, etc., and when such is the case one must proceed carefully before increasing the dose.

When the urine is extremely acid, loaded with urates, etc., one must first reduce the acidity of the urine. This is most easily accomplished by the use of **potassium citrate** in doses of 10 grains (0.6 Gm.) thrice daily—though larger doses may be required. When the acidity has been reduced, the belladonna should be begun. If the child's general health is not very good, 2 or 3 minims (0.12 to 0.18 c.c.) of **liquor strychninæ** added to the prescription is often beneficial. It is inadvisable to give meat when the child is suffering from this "acid" condition. When the urine is alkaline, contains pus, albumin, etc., **dieting** is of the first importance, all carbohydrate food as far as possible being prohibited. If the urine is very alkaline, **acid sodium phosphate** may be given; when the alkalinity of the urine has been reduced **belladonna** should be used in the manner stated above.

When bacilli occur in the urine a pure culture of *B. coli* is frequently obtained. If the urine is very acid it is wise to reduce the acidity by giving **potassium citrate**; then **urotropin** in 5- to 10- grain (0.3 to 0.6 Gm.) doses thrice daily often proves of immediate benefit. If there is mixed infection **salol** is often more efficacious. Mixed infection cases are often very troublesome, however, and a **vaccine** may sometimes be used with great advantage. Simpson (Edinburgh Med. Jour., Jan., 1913).

The urine is acid in only about 20 per cent. of incontinent children. In the remainder good results may be obtained from acidification with **phosphoric acid** (50 per cent.), 17 Gm. ( $4\frac{1}{2}$  drams); **sodium phosphate**, 34 Gm. (8 $\frac{3}{4}$  drams), and distilled water, 250 Gm. (8 ounces). One to 4 teaspoonfuls are taken before each of 2 meals daily and the treatment kept up for several weeks. Zuber (Bull. Soc. de péd. de Paris, July 22, 1922).

Habit, at times the cause of enuresis in children, may often be corrected by encouraging the cautious practice of holding the water.

The method of **conscious repetition of Brissaud** was found useful by the writer. He had the patient urinate at regular stated times, but every time he does so he is directed to void a little, say 2 drams, and then stop; then void 2 drams more and stop, and so on, until the bladder is emptied. In this way the individual exercises the mechanism which controls urination; he trains and educates himself in the voluntary execution of the act. After this has been done two or three times under the direction of the physician the patient can carry out the exercise, which should be persisted in. Herman (Archives of Pediatrics, Aug., 1910).

The **faradic current** is recommended. One electrode, a metallic sound or catheter, is passed into the urethra, and the other, a pad, is placed over the lumbar spinal cord. Hollowes (Pract., Nov., 1922).

Masturbation, phimosis, adherent prepuce, rectal affections, etc., must receive appropriate treatment, after which the incontinence of urine, if it persists, will demand attention. In some cases, the bladder is abnormally small and requires **mechanical dilatation**. Haven reported 2 cases in girls cured by gradual **distention of the bladder with a 4 per cent. boric acid solution**. Both were 18 years old, and from earliest infancy had wet the bed nightly, and found it impossible to retain the urine for more than a few minutes while awake. The bladder of both was abnormally small; that of the one held 8 ounces under pressure, that of the other only  $3\frac{1}{2}$  ounces. The treatment consisted in distending the viscus until discomfort was produced, after which the patient held the fluid as long as possible: ten to fifteen minutes in the beginning, though this time was doubled later. Distention was practised every other day, and improvement was rapid. Treatment was continued until the bladder would hold 20 ounces, and then, all symptoms having been relieved, it was discontinued.

Sir Henry Thompson strongly advocates the application of **nitrate of silver** to the urethra, whether in the male or the female. He states that the use of a **flexible bougie**, small, of course, for children, passed daily, and removed in a minute or so, is sometimes successful.

If this fails, the injection by means of a sufficiently long tube of the **nitrate-of-silver** solution to the prostatic portion of the urethra and neck of the bladder is a remedy of no mean value. For young women up to the age of 18 or 20 in whom this malady still exists, Thompson has found this

treatment almost invariably successful. It should be applied immediately after the bladder is emptied, in quantity, say, of a dram (4 Gm.), and of a minimum strength of 10 grains (0.6 Gm.) to the ounce (30 c.c.), up to treble that strength if necessary, for subsequent application. Enough should be employed to produce smarting, which should continue for a day or so. A week or two should elapse between each application.

Some authors advise **blistering the perineum**, others the use of the **actual cautery**, touching the same at several points around the anus.

According to White and E. Martin, when a habit of nocturnal incontinence is due originally to carelessness—the child, though awakened by the desire to urinate, preferring to wet the bed rather than get up—the case may be cured by having the patient waked at about 1 or 2 in the morning, or at an hour before the habitual time of involuntary micturition, and made to empty the bladder.

While **atropine** has a certain adjuvant value, it should be given rather liberally, for small doses are useless. When the habit, as often happens, is associated with a general run-down condition **tonics** are indicated. **Removal of adenoid vegetations** or greatly **hypertrophied tonsils**, if present, is indicated, but a conspicuous effect on the enuresis need not be expected, save that the operative shock or the anesthesia may check it, as it may any habit spasm. It is wise to continue the training for a considerable time, at least two months, after the incontinence has ceased. Wachenheim (N. Y. Med. Jour., Feb. 5, 1910).

In cases in which the cause cannot be discovered the writer recommends, in girls, catheterizing the bladder aseptically, and then **instilling** through the catheter 1 ounce (30 c.c.) of 3 per

cent. argyrol solution, letting some remain in the bladder for  $\frac{1}{2}$  to 1 hour, after which it is voided. This is done every day or every other day. The strength of argyrol is gradually increased until 10 per cent. is borne without irritation, which should be avoided. In boys, the argyrol is injected through the urethra with a bulb syringe, washing out the urethra with sterile water after the argyrol is driven into the bladder. W. R. Barrow (Jour. Amer. Med. Assoc., May 22, 1920).

Among other remedies employed in this affection are **antipyrine**, **rhus toxicodendron**, **potassium bromide**, **monobromated camphor**, and **ergot**.

With **ergot** I have had personal and very favorable experience.

The fluid extract of **rhus aromatica** has been recommended by Carpenter, Freyberger, and others. Freyberger's method consists in regulating the diet, advising the patient to sleep on a **hard mattress**, the use of light coverings, and **cold sponging along the spine**. The parents are directed to take their children up once or twice during the night, and to make them pass water.

The dose of rhus employed was:—

Five to 10 minims (0.3 to 0.6 c.c.) for children 2 to 5 years old.

Ten to 15 minims (0.6 to 0.9 c.c.) for children 5 to 10 years old.

Fifteen to 20 minims (0.9 to 1.2 c.c.) for older children.

A very convenient formula is:—

**R** *Ext. rhus aromatici liq.* . ℥x (1.2 c.c.).  
*Syrup. aromatici* . . . . . ℥xx (1.2 c.c.).  
*Aq. destillata* . . . . . ad 5j (4.0 c.c.).

Sig.: Three times a day.

Thirty-three days on an average were sufficient to produce a permanent cure; fifty-three days to effect a permanent improvement in about one-third of the cases treated.

Where abnormally frequent urinations are due to disturbances in the

bladder innervation, Fernand Cathelin, of Paris, devised the operation of **epidural injections of saline solution** and obtained good results.

Eight cases treated by the writers by Cathelin's method at the Manhattan Hospital West for the insane. All were adult women and had histories of wetting the bed and clothing frequently for some time previously. The injections are made into the sacral canal between the periosteum of the vertebrae and the dura mater. The canal is reached through its opening in the sacrum. The patient is placed in the Sims position, the area sterilized, and the small osseous tubercles just below and to either side of the last palpable sacral spinous process are made out. The needle of an aspiration syringe is then thrust through the skin, drawn tightly between these two tubercles, the needle being held at an angle of 40 degrees to the sacral curve until it passes through the membrane covering the opening of the canal, when it is lowered to 20 degrees and pushed on into the canal. Five cubic centimeters (80 minims) of sterile salt solution were usually injected at first and later 10 or even 15. These injections were made at intervals of about one week and favorable results followed immediately in all 8 patients in whom the injections were made. These cases have not been followed very long, but most promising results have thus far been obtained. The injections seem to be in nowise dangerous to the patient, and are no more painful than any hypodermic injection. The immediate effects are rarely even disagreeable. Valentine and Townsend (Med. Record, Sept. 26, 1903).

The writer obtained several favorable results by means of **rectorectal injections of normal saline solution** in amounts up to about 6 ounces (180 c.c.). The needle is inserted just anterior to the coccyx, a finger having been placed in the rectum in order to protect this viscus. To obtain the best results of the treatment several

injections may be necessary. It is indicated in those forms of incontinence of which the causation is not obvious. Jaboulay (*Tribune méd.*, vol. xli, p. 202, 1908).

Cathelin's method of injection of **salt solution** applied in 22 cases of involuntary micturition at night in children, and good results obtained in about half the cases. The writer is convinced, however, that the effect was due to suggestion and that probably equally good results can be obtained by the usual measures supplemented by suggestion without the necessity for the epidural treatment. Allaria (*Gaz. degli Ospedali*, April 27, 1909).

Subcutaneous injections of **saline solution** made in the anterior perineum, 60 to 70 Gm. (2 to 2½ ounces) being used at each sitting—enough to cause a swelling the size of an egg. The pain is very slight and the results are excellent, since adults who from infancy have been given to wetting the bed, awake with the desire to urinate, and do so without trouble, and into an appropriate vessel. Cahier (*Arch. de méd. et de pharm. militaires*, June, 1909).

A method introduced in 1901 consists of epidural injections of solutions of **cocaine** or **novocaine**. The Sims position is preferred for the injections, although the Trendelenburg or the knee-chest position may be used, and the site of injection is in the sacral region. Of 19 cases treated in this way by the writer all were completely cured. The injections are best made with 10 c.c. (2½ drams) of a 2 per cent. solution of novocaine given every 8 days. If the desired result is not obtained by 4 or 5 injections it is useless to persist. E. Pel-lechia (*Riforma Medica*, Jan. 23, 1915).

In a boy of 15 there was complete inability to control the evacuation of the bladder except by frequent micturition. No treatment having proved effectual, a perineal injection of 30 c.c. (1 ounce) of **physiological salt solution**, repeated the following week on the other side, cured the enuresis at 1

stroke. The patient has been normally continent since the first injection. Marion's technic was followed; the injections were quite painful. The writers have reported a case of complete recovery after a single perineal injection of 20 c.c. (5 drams) of the solution in a man of 25 with nocturnal enuresis from childhood. In Ortiz's 2 cases, no effect was apparent. Serantes and Montes (*Revista de la Soc. Arg. de Urol.*, Oct., 1925).

**Organotherapy** has given excellent results in well-selected cases, *i.e.*, those in which there is evidence of lymphatic temperament, hypothyroidia or deficient metabolic activity or oxidation as represented by weakness, pallor, puffiness, obesity or mental dullness—all of which symptoms or conditions may occur simultaneously. Sajous recommends **thyroid gland**, ¼ to ½ grain (0.016 to 0.032 Gm.) *t. i. d.*, having noted that many of these cases are subjects suffering from hypothyroidia. **Pituitary** and **adrenal** preparations have also been used with good results.

Of 134 cases of urinary incontinence treated with the substance of the **suprarenal gland**, 66 were cured, 21 were improved, 14 were better during the duration of the treatment, 21 were not changed; in 12 cases the statements were not sufficiently accurate for classification. The best results were obtained in those cases which came under treatment early, while a considerable share of the failures were due to deficiencies in the treatment, especially too short a duration.

The treatment should be interrupted for several days at a time, in order to guard against habituation, and the dosage of the remedy must not be too small. The only ill effects obtained by giving these preparations on an empty stomach were slight abdominal pain and a tendency to vomit. These symptoms promptly

subsided when the dose was diminished. Zanonì (Med. Standard, Nov., 1908).

Nocturnal incontinence of urine in young children and adolescents is due to thyroid insufficiency. Several cases in which the use of **thyroid gland** was followed by improvement or cure. Children who suffer from incontinence are almost always undersized, and they present the infantile habitus in varying degrees—improperly placed teeth, nasopharyngeal adenoids, flat chests, and emaciated and slender extremities. Such patients are often flat-footed and their feet have an offensive odor, their gait is stiff, they suffer from pains in the thighs and from sciatica produced by the cold and moist surroundings in which they lie at night. The systematic examination of the urine in these cases shows an abundant deposition of the cells covering the free surface of the mucous membrane of the bladder. In children beyond 2 years of age the writer gives three 5-grain tablets of thyroid extract each week with from 3 to 5 grains (0.2 to 0.3 Gm.) of **potassium iodide** and **bromide** daily. Hertoghe (Bull. de l'Acad. royale de méd. de Belgique, xxi, No. 4, 1907).

Series of 25 cases in which relief was afforded by means of small doses of **thyroid gland**. The suggestion was obtained from the case of a boy with nocturnal enuresis who instead of improving on removal of his adenoids and tonsils became worse. The therapeutic effect of thyroid extract "was most drastic." The enuresis ceased immediately and never recurred. It is important that the dose of thyroid gland be small—from  $\frac{1}{2}$  grain to  $2\frac{1}{2}$  grains (0.03 to 0.16 Gm.) thrice daily—as larger doses may defeat the purpose of the treatment, as was illustrated in one case in which enuresis previously absent developed in a boy to whom  $2\frac{1}{2}$  grains (0.16 Gm.) of thyroid extract were administered thrice daily for the correction of general debility following an attack of nephritis. The

initial dose should be small, and it should be increased only if necessary, but no more should be administered than the minimum sufficient to effect the desired result. Leonard Williams (Lancet, May 1, 1900).

Ten patients received the following treatment: One-fourth grain (0.016 Gm.) **thyroid gland** was given three times a day, increased to  $\frac{1}{2}$  grain (0.03 Gm.) three times a day. Fluids were not allowed after 4 P.M., and the foot of the bed was decidedly elevated at night. Of these 10 patients, 8 improved; 2 did not improve. Of the 8 who improved, in 4 cases circumcision had been previously performed without result. Fleischner (Calif. State Jour. of Med., Feb., 1911).

Enuresis is sometimes associated with a special form of infantilism or hypoplasia due to thyroid insufficiency. **Thyroid gland** in small doses— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 Gm.)—will usually relieve the enuresis. The dose should be decreased or omitted if rapid pulse, fever, or other toxic symptoms arise. In cases not responding well, alternate thyroid with **calomel**,  $\frac{1}{10}$  grain (0.006 Gm.) *t. i. d.* Relief is usually obtained in a month or two, but some cases require further medication to improve general condition. Also supervise child's **exercise, diet, bathing**, etc., and guard against physical or mental strain. McCready (Penna. Med. Jour., Jan., 1911).

Series of 28 unselected cases of enuresis were treated with **thyroid gland**. Of these 16 showed marked improvement or were cured, and 12 did not improve at all. As the children were only seen once weekly the drug was given cautiously, the initial daily dose being  $\frac{1}{4}$  or  $\frac{1}{2}$  grain (0.016 or 0.032 Gm.). The cases which appear to react to this form of treatment better than all others are those in which the enuresis has persisted since birth, and in which the patients are also backward. A. C. D. Firth (Lancet, Dec. 9, 1911).

The connection between nocturnal enuresis and adenoids has not been generally recognized. Out of 716

cases of adenoids operated on by Fisher, 14.8 per cent. were troubled with enuresis. Mygind reported 7.75 per cent. out of 400 cases and Gruback 14.28 per cent. out of 427 cases. Hamonic circumcised in 187 cases of phimosis suffering from incontinence of urine, with 130 cures. Of these, 47 were cured in 25 days, 83 within 42 days, and the remainder lost sight of. Ruhrah (*Amer. Jour. Med. Sci.*, Feb., 1912).

Recovery of 8 out of 12 children obtained, and great improvement in 3, by injections of **pituitary extract**. Bonacorsi (*Pediatrics*, Sept. 1, 1925).

The application of **collodion** over the opening of the urethra has, in Somway's experience, been found effective in cases of nocturnal enuresis; the pressure of the urine awakens the child, and it thus becomes gradually weaned from the habit of bed-wetting.

The injection of **paraffin** parallel to and along the urethra, or around this canal, a method introduced by Gersuny, has been found of value in relaxation of urethra, loss of tone of the sphincter, laceration or lesions compromising its efficiency as a canal.

Case of a woman who had been subject for six years to incontinence of urine, apparently of traumatic origin. It became so complete as to prevent her working for a living. There was a posterior colpocele without prolapse of the anterior vaginal wall; the uterus lay a little below the normal level. The urethra was intact, but its sphincter had lost its normal tone. In order to narrow the relaxed urethral canal and to afford a resisting medium upon which the sphincter might act, the author injected solid **paraffin** into the urethral canal after Gersuny's method. The incontinence disappeared in a few days, and did not return. Fabre and Trillat (*Ann. de Gynéc. et d'Obstét.*, Sept., 1908).

Two cases of complete cure of hitherto intractable cases of incontinence of the urine in women. In the first patient, one injection of the ordinary commercial **paraffin** parallel to and along the urethra sufficed; in the second, three injections were necessary. E. H. Eising (*Med. Rec.*, April 27, 1912).

The enuresis which occurs after labor as a result of prolonged pressure, traumatism, etc., usually subsides as resolution of the parts take place, and without treatment. In some cases, however, the enuresis not only persists but increases. A careful examination of the pelvic organs is then necessary and whatever morbid condition is found demands remedial procedures, often on surgical lines.

The nature of the operation should depend upon the condition of the urethra and bladder neck. The **Frank operation**, combined with an anterior and posterior colporrhaphy in cases where there is a relaxed and gaping vagina, and some appropriate operation for retroversion where this exists, will cure the average case of incontinence coming on after labor, and of not too long standing. In cases where there is a marked dilatation of the urethra and of long standing, or cases where from necrosis the muscular wall of the neck of the bladder and urethra are wanting, **Gersuny's operation** seems to offer the best hope of cure. **Pawlik's** and **Dudley's operations** have likewise given good results at the hands of their originators. G. Brown Miller (*Surg., Gynec. and Obstet.*, Jan., 1910).

In 2 cases of incontinence of urine in women due to stretching or trauma of the urethra and surrounding tissue, in which numerous methods of cure had been tried without success, the writer obtained complete recovery by **cauterization** of the **internal vesical sphincter** through Caspar's operating cystoscope. Two or three deep grooves were burned in the



sphincter at the point of transit from the bladder to the urethra. Caspar (Zeit. f. Urol., II Beiheft, 238, 1912).

A **plastic operation** on the internal and external **sphincters** is effective in cases of incontinence of urine of long duration where both internal and external sphincters have been destroyed by previous operative trauma. Young (Surg., Gynec. and Obstet., Jan., 1919).

The writer has had good results in 18 cases with an **operation** consisting of the isolation on careful dissection of the layer of fascia and muscle forming the external sphincter of the bladder, and its careful resuture. In 1 type of case, **plication of the vesical sphincter** is also carried out as the first step in the operation. E. L. Young, Jr. (Jour. Amer. Med. Assoc., Nov. 18, 1922).

Of 24 patients with enuresis operated upon, in 21 the X-ray showed spina bifida. Operation revealed in every case a fibrous band bridging the gap and compressing the dural cul-de-sac and the nerves of the cauda equina, affecting chiefly the sensory fibers. This yellow band ligament was found not only in the lumbar region but also in the sacral, evidently due to defective union of the sacral vertebrae or to the persistence of the ligament in apparently united vertebrae. The operation consisted in resection of this band. There were one and sometimes several of these bands. Ten patients were cured; ten were only slightly improved; in three the results were negative. The writers regard this band as responsible for the enuresis. All with purely nocturnal enuresis were cured. The failures were all in patients with chronic nervous or mental disease or a history of some urogenital disease. The scar of the operation is liable to induce recurrence by its pressure. Delbet and Lévi (Revue de Chir., lxi, 483, 1925).

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**EPHEDRIN.**—Ephedrin, according to T. G. Miller (Amer. Jour. M. & J. Sci., Aug., 1925), has general physiological effects in

man similar to those produced by epinephrin. It has, however, distinct practical advantages over epinephrin because of its more prolonged action and the fact that it can be administered effectively by mouth. Miller reports his clinical observations with this drug. In doses of from 50 to 125 mg. ( $\frac{3}{4}$  to 2 grains), given orally or subcutaneously, ephedrin sulphate usually raises the systolic and diastolic blood-pressure and decreases the pulse rate for a period of several hours. It also stimulates the heart action and has a tendency to increase the output of urine. It sometimes increases the basal metabolism.

Its administration caused temporary improvement in 2 cases of **Addison's disease**, gave relief in the paroxysmal attacks of certain cases of **asthma**, relieved the subjective sensations in a case of **urticaria**, caused a disappearance of **urticaria** in a case of serum disease, and produced marked temporary improvement in a case of **circulatory failure** incident to myocardial disease and the evacuation of an overfilled urinary bladder. In a single case of complete **heart block** it produced an increase in both the auricular and the ventricular rates and caused alterations in the character of the electrocardiographic tracings.

Locally applied to the nasal mucous membrane, ephedrin causes prompt contraction which persists for more than 3 hours, and has no local irritant effect. It is believed that a wide range of usefulness of ephedrin will be found in the treatment of asthma and of acute circulatory depression, as well as in the management of certain congestive nasal conditions.

**EPIDIDYMITIS.** See PENIS AND TESTICLES, DISEASES OF.

**EPILEPSY** (Morbus Sacer; Falling Sickness).

**DEFINITION.**—Epilepsy may be defined as a disease characterized by the habit of having convulsions, attended usually with unconsciousness, the seizures occurring suddenly and at irregular intervals, the subject showing an essential tendency to progressive mental and motor weakness.

**VARIETIES.**—The generic term epilepsy is applicable to and includes numerous subtypes, some of which differ from each other symptomatically and otherwise most markedly; hence the necessity for a classification of varieties. We have, for example, a division into two forms expressive of a difference in the degree and intensity of the motor spasm and impairment of consciousness in the attack—major and minor epilepsy, or, as the French express it, *grand* and *petit mal*. Other synonyms are general and partial, and, in a more restricted sense, frank or masked epilepsy. In *grand mal* both consciousness and motor spasm are involved in profound degrees. In *petit mal* both consciousness and motor spasm may be only slightly and transiently involved. In *general* epilepsy the motor spasm may involve all the muscles of the body and the loss of consciousness may be absolute. In *partial* epilepsy only one extremity or even one set of muscles may be affected and consciousness only slightly if at all perceptibly impaired.

Partial epilepsy is, perhaps, more readily recognizable under the name *Jacksonian*, or cortical, epilepsy: terms more popular, since they embody facts of etiological and pathogenic, as well as symptomatic, significance. The term “cortical” is, however, utterly indefensible here, since we have good reason to believe that all epilepsies are essentially of cortical origin. In *masked (larvated)* epilepsy there may be neither motor spasm nor apparent unconsciousness, but certain phenomena of abrupt onset in the psychical or motor volitional sphere may occur which, by reason of their habitual recurrence in the same or similar form,

constitute a variety of the disease; automatic, causeless, but apparently purposive movements may represent the entire motor explosion. A transient stupidity or “absence of mind”—perhaps a random or irrelevant remark—may be the only evidence of impaired consciousness. Certain vasomotor disturbances, such as pallor, flushing, etc., usually accompany attacks of this character. In certain cases, first described by Weiss and to which he gave the name “psychical” epileptics, the explosion is, objectively at least, entirely in the direction of disturbed mental equilibrium, such patients being subject to irregularly and abruptly recurring paroxysms of transient insanity, usually with an aura, or warning, and with no recollection subsequently of the attacks. Such seizures, as well as other less-marked, but irregularly recurring psychical disturbances, are described by other writers as *epileptic psychical equivalents*. Special interest attaches to this subvariety of masked, or larvated, or psychic epilepsy, from a medicolegal standpoint, on account of the potentially criminal possibilities of such individuals during an attack.

The element of periodicity in the time of occurrence of the attack, a factor of some importance in both prognosis and treatment, has served as the basis for a chronological division into *diurnal*, or day, and *nocturnal*, or night, epilepsy, the former being still further divisible into the matutinal, or morning, and the vesperal, or evening, cases. In the succeeding paragraphs upon symptoms we shall find evidence of the necessity for a further elaboration of subtypes.

**SYMPTOMS.**—The symptom-picture in epilepsy varies quite widely, as

has been intimated in the classification and description of subtypes. Not only is there a marked difference symptomatically in these clinical sub-varieties, but each individual patient may differ in some major or minor particular from all others, although preserving in each instance some essential factor revealing a common identity. In typical *grand mal* the patient, with or without an aura or warning is suddenly seized with a convulsion, attended with unconsciousness of greater or less degree. There is simultaneously a sudden alteration in color, either lividity or pallor, and the unconsciousness may be preceded or attended by an involuntary cry or scream. The patient falls unconscious regardless of surroundings; the muscles of the face and extremities become extended in rigid tonic, followed quickly by clonic spasm; frothy saliva, sometimes mixed with blood, escapes from the mouth; breathing becomes labored or stertorous from spasm of the respiratory muscles; the sphincters relax, allowing involuntary escape of urine, feces, and sometimes semen; the whole convulsive attack lasting from a few seconds to ten minutes or longer. This convulsion is followed, in typical cases, by a deep semicomatose sleep, lasting from a few minutes to several hours, the patient on awakening remembering nothing or very little that occurred after the onset of the convulsion.

Slow pulse, vasomotor stasis in the extremities, tendency to obesity and bulimia, are suggestive of pituitary disorder. Clark and Caldwell (Jour. Amer. Med. Assoc., Jan. 3, 1914).

An intensive study of a case of epilepsy based on notes of 500 examinations in which the reflex vasoconstriction reaction times and the reflex

vasoconstriction valuations were carefully recorded, showed the following: Chronic vasoconstriction spots which varied in color and becoming white at times; abnormal reflex vasoconstriction phenomena, anemic dermography on striking the skin, indicating adrenin in the blood; increased tonicity of sympathetic fibers, preceding convulsive seizures, as shown by the short reaction time; abnormal face reflexes; hypercontent of adrenin in the blood; lowered content of lime in the bones. E. A. Tracy (Interstate Med. Jour., vol. xxiv, No. 5, 1917).

In atypical cases any one or several of these symptoms may be absent or so slight as to be scarcely noticeable. In some patients one or more of these symptoms may be replaced by substitutive conditions entirely different. In *grand mal* the postconvulsive somnolence may be replaced by an outburst of excitement or delirium or by states of altered personal identity in line with the theory of dual consciousness during which actions both embarrassing and reprehensible may be committed, involving sometimes grave questions of medicolegal responsibility.

In *petit mal* both motor spasm and unconsciousness are involved in far less degree, as the term indicates. Very often, indeed, the disturbance is of one sphere alone apparently, the attack consisting of a transient loss of consciousness alone, without motor spasm, or of motor spasm unattended with perceptible loss of consciousness.

Not only may the motor spasm occur alone; it may be further limited to one limb or to one set of muscles, or even to a single muscle. Such limited spasms are, however, observed—we have reason to believe—only in the organic epilepsies belonging to the Jacksonian, or so-called cortical,

group. In such cases the limb or muscle involved points with localizing significance to the site of the disease-process in the corresponding center in the cortex. This statement is true, though of less value, as regards the various forms of sensory and psychical epilepsy. Among the rare clinical forms of atypical epilepsy most of which are of the *petit-mal* group are *epilepsia procursiva*, *E. nutans*, *E. loquax*, cardiac epilepsy, and migrainous epilepsy. *Epilepsia procursiva* is a form of the disease in which "the attacks consist in a straight or circling run, of a variable distance, which is rarely followed by a fall or cry, but by facial congestion" (Hare). The patient may run to the left or right or straight ahead. The act is essentially involuntary, of course, though absolute unconsciousness may not occur. This purposeless run may constitute the entire clinical phenomenon; it may represent the first stage of an ordinary epileptic attack; it may occur as a postepileptic phenomenon.

In *epilepsia nutans*, a minor form of Jacksonian epilepsy, the motor spasm is limited to the muscles of the neck, causing nodding of the head alone. In *epilepsia loquax* the attack consists in an explosion of speech, the focus of disease being presumably limited to the speech-center. I have seen personally only one case of *epilepsia loquax* among several thousand epileptics observed during the past twenty-five years. In cardiac epilepsy the attacks at first may resemble closely either angina pectoris or simple cardiac syncope. The patient has little more than an aura of precordial anxiety, usually at night, or when lying down with transient consciousness, but without motor

spasm. There is in such cases either a bradycardia or a tachycardia, rarely a normal pulse, usually no organic cardiac disease, but often some arteriosclerosis.

Attacks of tachycardia or bradycardia may last for hours, days, or weeks. After a variable interval the heart tends to become exhausted, and irregularity occurs—in short, heart block takes place. Stops are felt in the radial pulse, and concurrently nervous symptoms arise which vary from the slightest feelings of sparks flashing before the eyes or the waving of a sheet before the patient, to severe epileptiform convulsions, with loss of consciousness. Yet such attacks are most certainly not epileptic. From the writer's study of such cases he concludes that tachycardia is a pure neurosis, characterized by a great increase in auricular contractions from disturbed nervous influences. Clarke (*Brit. Med. Jour.*, Aug. 10, 1907).

Five cases illustrating cardiac neuroses or cardiac epilepsy, attended with or followed by distinct angina pectoris. Newton (*N. Y. Med. Jour.*, June 26, 1909).

Bárány's sign, conjugate deviation of the eyes, present in 23 out of 50 cases. The writer concludes that Bárány's sign is not constant in epilepsy, when found. It is not rare in apparently normal children. Tracy (*Boston Medical and Surgical Journal*, June 21, 1917).

It is at first a *petit mal*. Gradually, as a rule, the attacks become more severe, and finally may assume the major, or *grand mal*, type. This fact of transition in these milder forms to the severer forms of the disease is true of all cases as a possibility, although in many patients a *petit mal* remains such. The interchangeability as regards type is one of the many curious and inexplicable phenomena observed in this affection.

Migrainous epilepsy is a form of the disease in which habitual migraine may be either succeeded by true epilepsy of major or minor type or the epilepsy be succeeded by migraine, or the two conditions may alternate in the same patient. In some instances many phenomena of both diseases—if they be really two—may be noted simultaneously. I have seen two such instances.

The frequent co-existence of epilepsy and migraine emphasized. Usually the epilepsy appears later than the migraine. One of the conditions, however, cannot be mistaken for the other. Where such a condition might have existed, the migraine proved to be a symptom only of the underlying epilepsy, or the epilepsy appeared as a new element in addition to the migraine. Strohmayer (*Munch. med. Woch.*, March 10, 1903).

Abnormalities of cardiovascular phenomena occur in the vast majority of epileptic seizures. Removal of enlarged veins or nevoid growths adjacent to the base of the skull has caused cessation of seizures. Epilepsy causes circulatory disturbances, and abnormalities of blood or vessels cause epilepsy. T. E. Satterthwaite (*Trans. Amer. Therap. Soc.; Med. Rec.*, Sept. 23, 1916).

In studying the peculiarities of attacks in individual examples of the disease it will be found of advantage to systematize such study under four divisions or stages: the preparoxysmal, the paroxysmal, the postparoxysmal, and the intraparoxysmal or inter-valling period, as it is sometimes called.

The preparoxysmal, or pre-epileptic, stage covers the period immediately preceding the attack. By far the most important symptom to be investigated here is the aura, or warning, by which is meant some

peculiar and constant subjective sensation or psychological impression realized by the patient as being premonitory of a fit. An aura is present in less than one-half of all cases, but it may be of great value and should always be carefully investigated. The aura may be referable to any of the senses. Flashes of light, sudden blindness, weird and fantastic visions, strange noises, tinnitus, deafness, numbness or tingling, or burning or pain in the extremities; disagreeable and indefinite, but constant stomachic sensations—as fullness, oppression, or pain; constriction of the throat, or of a limb, or of some part of the trunk—are among the auræ which have been noted.

The aura is an aid sometimes in deciding the etiological diagnosis. A sensation of coldness preceding an attack is said to be, especially if associated with subnormal temperature, almost diagnostic of cardiac epilepsy. A warning of precordial anxiety is also suggestive of this type. The aura often constitutes a guide to the location of the cerebral lesion, as, for example, in the patient reported by Beevor and Horsley, in whom an aura of a horrible taste and smell pointed to the uncinate and hippocampal gyri (see also Hughlings-Jackson), found to be the site of the causative lesion upon post-mortem examination. The interval between the aura and the attack varies. At times it is exceedingly short; in others the interval is sufficient to permit the patient to prepare for and prevent the attack. Other preparoxysmal warnings of an impending attack occasionally noted are headaches, vertigo, great irritability, stupidity, and quite frequently a ravenous appetite.

The irritability and impatience noted in many epileptic subjects is often supplemented by an excessive mobility of temperament. At one time depressed, hypochondriacal and convinced that he will never recover, at another the epileptic will show a sanguine and happy disposition. Often he is well satisfied with himself, and is fond of giving advice to others: at times he is cunning and jealous, and again he becomes unduly religious. It is the same with his actions: whilst sometimes prompt to carry out orders and willing to be of service, he is often dull, stupid, idle, and prone to refuse work. These characteristics are, however, neither limited to the epileptic nor necessarily to be found in every case, and a series of observations are recorded in some of which confirmed epileptics have shown a normal mentality, and in others the so-called epileptic character has been met with in feeble-minded or imbecile patients, and in cases of dementia precox and general paralysis. L. Marchand and H. Nonet (*Revue de méd.*, Nov. 10, 1907).

The naughtiness, the moodiness and brutality shown by certain children who develop epilepsy later; he regards this abnormal behavior as an early manifestation of epilepsy. Stadelmann (*Med. Klinik*, Dec. 25, 1910).

Case with seizures starting by a visual aura (blue) in a hemianopic region (right lateral homonymous hemianopsia), with anxiety and palpitation. In the interval between seizures, there were numerous epileptic equivalents with colored hemianopsia. Cases of hemianopsia can have in the blind field abnormal light sensations of different kinds: visual hallucinations, scintillating scotomas, and colored rays. The different symptoms of irritation of the half-blind visual sphere may be transitory or may persist throughout the duration of the hemianopsia. Henri Roger and Reboul-Lachaux (*Encéphale*, Dec., 1921).

The paroxysmal stage should always, if possible, be studied person-

ally, or through a competent trained observer or nurse. The statements of the patient are obviously unreliable. The most important phenomenon to be noted in this stage is the location of the first convulsive movement, or, as it is called, the signal symptom. This initial motor spasm, close in significance to the aura, is even more valuable at times in pointing toward the cerebral area involved by the lesion. Spasms, always beginning in the right foot, for example, point to the upper left Rolandic cortex, etc. The value of the signal symptom is greater the earlier it is recognized. Epilepsy of long standing, even though dependent upon a focal lesion, tends to become general. In old epileptics the signal symptom may actually appear to originate in the sound side, cortical irritability having become exhausted by prolonged insult of the originally affected hemisphere.

The postparoxysmal period is quite as important for the determination of essential facts as either of the other two and in much the same way. A monoplegia,—or limited sensory loss,—an aphasia, or an acute psychosis may possess an even more positive pathogenetic and localizing significance than the aura, or signal symptom.

Following one or more epileptic seizures of either type there may be a considerable period during which there are delusions of a more or less fleeting and temporary character. Such delusions are rarely fixed. They appear mostly in the form of accusations against attendants or fellow patients, charging the administration of poisons in the food or in medicines or abuse, resulting in the bruises, etc., which are really the result of falls. The mental disturbance is seldom of

so severe a nature as to cause acts of violence, although acts of sexual perversion are not uncommon. Gradually the delusions disappear and the patient resumes his usual mental condition. W. H. Pritchard (Ohio State Med. Jour., March, 1910).

The interparoxysmal period is quite interestingly filled with curious phenomena in many cases. Various states of mental alteration or abnormality, of amnesia and morbid propensity, may appear, and may decide entirely the question of prognosis. It is this stage perhaps which is of most interest and importance in determining the medicolegal status of the criminal epileptic, although epileptic crimes of violence usually occur in the postconvulsive period. Evidences of essential degeneracy, manifest in stigmata, are conveniently considered here.

The psychoses of epilepsy have very definite and immediate associations with other manifestations of the disease. The plea of irresponsibility for criminal acts alleged to have been committed while an individual was suffering from epileptic mental alienation should be considered invalid, unless other and irrefragable manifestations of the disease can be adduced. The vague and ill-defined convulsions, which date back to infancy or early childhood, do not constitute such other manifestations. J. W. Courtney (Med. News, June 22, 1901).

The *paranoid* type of epileptic dementia is characterized by systematized delusions, ideas of persecution, loss of all the sentiments of affection, convulsive paroxysms, and attacks of violence, especially at the menstrual periods. The *catatonic* type is characterized by catatonic stupor, suggestibility, verbigeration, and negativism, which may go so far that the patient refuses to eat and has to be fed by gavage. The course is more rapid in this form than in any other.

Two theories as to the origin of epileptic dementia predominate: 1, that the dementia is due to the epilepsy, all the nervous phenomena of epilepsy are thought to be due to a cerebral irritation of toxic origin; 2, that the dementia is due to degeneration, traceable back to heredity. Voisin (Revue m  m. des mal. de l'enfance, Aug., 1907).

Some epileptics show an asymmetry to Weber's tactile sensibility seen only in patients suffering from organic nerve disorder. Asymmetry is found in sound persons, but not in persons suffering from a functional disease and only in those suffering from organic nerve disorder or idiopathic epilepsy. This symptom has not always the same significance. Its origin can be explained in three ways: It may be the sole symptom of cortical epilepsy occasioned by a focus in the cortex; it may be a manifestation of an asymmetrical development of the cerebrum which might be the constitutional condition of idiopathic epilepsy itself; it may be the symptom of a secondary change in the cortex, caused by those physiologic changes which are associated in idiopathic epilepsy and may become settled after some recurrences of attacks. In from 25 to 30 per cent. of epileptics it gives a rapid diagnosis without observation and without the provocation of a seizure. L. Focher (Jour. of Nerv. and Mental Dis., Oct., 1925).

Asymmetry or abnormality of development, especially of the skull; undue elevation of the palate roof (Gothic arch), a deficient number of teeth, undue elongation or eversion of the coccyx,—the rudimentary tail of F  r  ,—are among the large number of stigmata observed.

There are characteristic functional stigmata in the voices of persons suffering from nervous and mental diseases. The characteristic speech of paresis and the thin, high-pitched voice of paralysis agitans are well known and readily recognized by all. Many of us have observed that there

is something very peculiar and distinctive in the epileptic voice, which is expressionless, and renders the epileptic incapable of singing beautifully or speaking well. Clark and Scripture (*Med. Record*, Oct. 31, 1908).

Early objective phenomena are: (1) Imbalance of the vasoconstriction reflexes on opposite sides of the body; (2) hypertonia of sympathetic fibers (manifested by the intensity in color of the reflex vasoconstriction, or by the reflex appearing sooner than normal); (3) a patchy reflex vasoconstriction, or the absence of the reflex; (4) chronic vasoconstriction spots. E. A. Tracy (*Med. Rec.*, Mar. 11, 1922).

**DIAGNOSIS.**—The recognition of epilepsy, in its typical form, is ordinarily a matter of no great difficulty. As, however, convulsions from uremia, dentition, etc., do not differ materially from epilepsy except in the matter of habitual repetition, it is necessary to consider all the collateral facts in addition to the seizure itself. A history of repeated convulsions of abrupt onset and without immediate assignable cause is, in itself, almost diagnostic. Even with such a history, however, the individual patient should always be given the benefit of a cautious differential examination, which should invariably include a careful uranalysis. Aside from the accidental or incidental convulsions which may accompany other diseases, such as nephritis, diabetes, certain forms of meningitis, brain tumors, etc., there are only four conditions which are apt to confuse diagnosis: tetanus, malingering, syncope, and hysteria.

There are a number of rapidly growing adolescents who have relatively benign fainting attacks which at first seemingly simulate larval forms of petit mal epilepsy. They are to be differentiated from this lat-

ter condition by the absence of the epileptic character and the general physical and mental stigma of the grave disorder. The syncopal states are but a part of the obscure clinical picture of dyspituitarism, in which there appears to be an excessive functioning of the anterior lobe of the pituitary gland. Coincident with the fainting attacks may be low blood-pressure, slow pulse, vasomotor ataxia, and a host of defective muscular and skeletal displacements. In the psychical sphere one may encounter not infrequently character delinquencies and slow mental development. The line of corrective treatment is physical plus the administration of specific glandular substance. Mild cases recover of their own accord by gradually restoring the glandular and physical balance, but they can be materially helped by proper direction and rest. L. Pierce Clark (*Amer. Jour. Med. Sci.*, Feb., 1922).

**Tetanus** differs from epilepsy in the two facts of retained consciousness and tonic spasm alone, clonic spasms being absent.

**Malingering.**—The detection of malingering will in some instances, as in the famous case of Clegg, the "dummy chucker," prove quite difficult. It is seldom the case, however, that a malingerer will learn his part as well as Clegg, and few of them will have the stoicism to withstand the tests of pinprick, hot iron, ammonia vapor, etc., which are indicated in suspected cases. I have more than once arrested the fit in a malingerer by firm pressure with the thumb against the exposed nerve at the supraorbital notch, and in one instance temporarily arrested the succession of fits in a status epilepticus. Clegg, by the way, was brought to an acknowledgment of malingering by being confronted with the fact that in his spasms he violated



a physiological as well as a physical law, in that the thumb was contracted in flexion *outside* instead of *inside* the other fingers.

**Syncope.**—In simple syncope there is no motor spasm.

**Hysteria** is really a form of malin-gering, and the same tests apply. Here, as with other manifestations of hysteria, the disease-picture simulated is nearly always overdone. A strikingly constant physiological mistake of the hysterical is the reversal of the epileptic order of the convulsive movements, beginning with the clonic instead of the tonic, or mixing them up indiscriminately. If the patient happens to be a woman and of any of the Latin races (and I would add Polish Jews) it is necessary to exclude, with special and elaborate caution, major forms of hysteria. In many forms of minor epilepsy, especially in cases in which the disease manifests itself through the medium of psychical or sensory equivalents, a positive diagnosis is possible only after continued and close observation.

Gowers attaches considerable importance to attacks resembling hysteria, which sometimes occur as sequelæ to epileptic seizures, especially of the minor type. Certainly the association of epilepsy and hysteria in asylum practice is not uncommon. Contortions of the most violent nature accompanied by animal noises and attempts at biting, etc., are frequent. W. H. Pritchard (Ohio State Med. Jour., March, 1910).

Referring to the differential diagnosis between hysteria and epilepsy, the writer found that in soldiers brought to the hospital with a history of attacks supposed to be epileptic, hypnotism was valuable to determine the character of the attack. The hysterical patient at the word of command reproduces the complete attack

in all its details, whereas the epileptic, though he may carry out all the commands, shows no reaction. Gen'l Staff, War College (U. S. Naval Med. Bull., July, 1918).

Cardiac epilepsy cannot, in its incipency, in some cases, be differentiated from angina pectoris. The association of arteriosclerosis or other evidences of vascular degeneration, common to both conditions, adds to the confusion. True convulsions, too, have been noted in association with the Stokes-Adams syndrome. Epilepsy occurring only at night may exist for years unrecognized. Sleep-walking, night terrors, persistent nocturnal enuresis, and other similar phenomena should always suggest an inquiry as to the existence of epilepsy.

Syphilitic epilepsy may be recognized from the history of infection, together with a history of the symptoms, which are, with remarkable constancy, premonitory of syphilitic invasion of the brain. Unless the epilepsy develops in early or middle life, without other assignable cause,—the first convulsion having been preceded by periodically recurring headaches of evening onset and nocturnal exacerbation, associated with marked insomnia, or, less often, somnolence, with general malaise, and irritability of temperament,—the diagnosis of syphilis, as a source, should be rejected in spite of a history of infection. If this prodromal syndrome be present, it should be strongly entertained in spite of a denial of infection. The employment of the Noguchi or Wassermann test should be a routine procedure in suspected cases. The possibility of the convulsive form of paresis should never be overlooked, especially in patients developing convulsions in adult life.

Eight cases, out of a large aggregate of colony material, in which myoclonus occurred as a complication. In one case, a male aged 16, in which the epilepsy was due to fright, the myoclonus appeared as a complication of epilepsy about two and a half years later. G. Weiss (*Jour. Nerv. and Ment. Dis.*, March, 1907).

The writer called attention to the presence in certain cases of an overgrowth of the anterior and posterior clinoid process, which overlapped the pituitary body, as shown by radiography, and suggested a relationship between this anomaly and epilepsy. C. C. Johnston (*Jour. Amer. Med. Assoc.*, Nov. 1, 1913).

In a study of epilepsy from the X-ray standpoint, based on 95 cases, the writer found 7 to be pituitary tumors without bony thickening, but instead local thinning of the body of the sphenoid or the clinoid processes from pressure was almost constant. In 16 cases there was local thickening of bony tissue confined to the clinoid processes, or to the anterior fossa of the base of the skull. In 22 cases it was found in two situations, namely, the clinoid processes and the base of the anterior fossa. In 35 cases there were bony changes in the clinoid processes, the anterior fossa and the body of the sphenoid bone. In 15 cases no bony alterations were found. McKennan, Johnston and Hemminger (*Jour. Nerv. and Mental Dis.*, Aug., 1914).

The sellas from a series of unselected epileptic subjects examined by the writer presented a wide variation in type, but the bony changes present seemed similar to those of non-epileptic cases. There was no characteristic change to be seen in epileptic sellas, though they appeared smaller. Munson (*Arch. of Internal Med.*, Apr., 1918).

**ETIOLOGY.**—Heredity, age, sex, occupation, and the history of previous or coexisting disease, or injury, are all factors demanding investiga-

tion in determining the etiology in every case of epilepsy.

Among 1473 epileptics in the Craig Colony, the writer obtained a positive Wassermann reaction in less than 2 per cent. Shanahan, Munson and Shaw (*N. Y. Med. Jour.*, Apr. 29, 1916).

Heredity is remarkably common as an etiological factor, especially in idiopathic epilepsy.

A study of the pedigrees of 177 families containing epileptics showed the following facts: A great similarity of behavior in heredity supporting the hypothesis that each is due to the absence of a protoplasmic factor which determines complete nervous development and that the nervous conditions named migraine, chorea, paralysis, and extreme nervousness behave as though due to a simplex condition of the protoplasmic factor which conditions complete nervous development, *i.e.*, persons belonging to these classes usually carry some wholly defective germ cells. Such persons may be called "tainted." When such a tainted individual is mated to a defective about one-half of the offspring are defective; when a simplex normal is mated with a defective about half the offspring are normal, the other defective or neurotic; when both parents are simplex in nervous development and "tainted" about one-quarter (actually 30 per cent.) are defective, and the proportion of tainted offspring is not noticeably higher when both parents show the same nervous defect. Normal parents which have epileptic offspring usually show gross nervous defect in their close relatives, and while we recognize that "epilepsy" is a complex, yet there is a classical type numerically so preponderant that, in the mass, "epilepsy" acts like a unit defect. Data point to a poisoning in slight degree of germ cells by alcohol, but the evidence is hardly crucial. There is evidence that in epileptic strains the proportion of epileptic children in the latest complete gen-

eration is double that the preceding. C. B. Davenport and D. F. Weeks (*Journal of Nerv. and Ment. Dis.*, Nov., 1911).

Heredity is variously estimated as present in from 15 to 50 per cent., Hamilton believing that it exists in one-half of all cases. It should be borne in mind, however, that he included immediate and collateral ancestral phthisis and apoplexy as evidences of heredity, which is not admitted by most clinicians. Epilepsy itself in the parent or grandparent or brother or sister is quite frequent. I have found parental epilepsy alone in 15 out of 77 cases. Many observers have found a much larger percentage. Insanity, migraine, alcoholism, consanguinity of parents, and major hysteria are among the more common ancestral taints observed. Migraine in the parent is, in my experience, far more frequent in the direct heredity of epileptics than is indicated in the literature. In Gowers's table of 1450 cases heredity appeared in the history of 36.6 per cent. As to age, epilepsy is peculiarly, though not exclusively, a disease of childhood and early life.

To determine to what extent epilepsy is transmitted directly from parents to offspring 33 matings resulting in 133 offspring, were studied. Of these 86 are living and 47 dead. Of the total 133 offspring there is a history of convulsions in 10, five having died in infancy, during seizures, two becoming arrested cases, and three confirmed epileptics. The group of living offspring contains 46 cases still under 20 years of age. The writer thinks it is not probable that 50 per cent. of these will develop epilepsy, while in the cases over 20 years of age heredity will play a much less important part. The results of his earlier work have been to a large degree substantiated and

his conclusion that epilepsy is less often transmitted directly from parent to offspring than we have heretofore been led to believe seems to be justified. D. A. Thom (*Boston Med. and Surg. Jour.*, Oct. 26, 1916).

Of Gowers's cases, 422 occurred under the age of 10 years, and 1087 under the age of 19 years.

According to the same table, females show a somewhat greater predisposition to the disease than males (females, 54.6 per cent.; males, 46.4). This relative difference is really greater than is indicated by these figures, if we take into consideration the greater exposure in males to cranial and other accidents, which are frequent causes of epilepsy. The occupation is often a sidelight upon the etiology. Epilepsy in sailors or prostitutes suggests syphilis; liquor-selling suggests alcoholism; painting and plumbing suggest lead as a cause.

Study of the pedigrees of 78 cases at the Monson State Hospital, and also those of allied families, making 90 pedigrees in all. The results are summed up as follows:—

1. We have no conclusive evidence that alcoholism in the parents is a cause of epilepsy in the children, although alcoholism is often associated with epilepsy. It may be regarded as a concomitant of epilepsy and an additional evidence of nervous weakness.
2. Feeble-mindedness is also associated with epilepsy, and there is some evidence that it is caused by the same defect that caused the epilepsy.
3. Fitting the material to the two hypotheses, first that epilepsy is a recessive trait that is inherited only as epilepsy, and second, that epilepsy, feeble-mindedness and insanity are due to the same defect which may appear in the form of any one of them, there is no striking evidence in favor of one to the exclusion of the other. The truth probably lies somewhere between the two. Flood and

Collins (*Amer. Jour. of Insanity*, January, 1913).

The writer observed a family of 30 members in 4 generations, 11 of whom have no sense of smell, 4 very little, while 2 members of the later generation are epileptics. The anosmia was transmitted through the women. This connection between anosmia and epilepsy should suggest study of the hippocampus major in epileptics and in persons suffering with anosmia. Alikhan (*Schweizer med. Woch.*, Mar. 11, 1920).

Certain diseases tend to develop an instability of the nervous system, and thus predispose the subject to the subsequent development of epilepsy.

The various forms of epilepsy, including that which appears to be of emotional origin alone, and the mixed varieties formerly classed as hysterio-epilepsy, are the result of not one, but several co-existing factors, of varying relative importance and variously combined. Among these, however, three may be said to predominate: The cortical trouble, evidences of which may be detected even in emotional cases; the general toxic factor, usually of gastrointestinal origin, and circulatory instability, especially such as is manifested in sudden marked alterations of equilibrium in this system, which may be the result either of physical exertion or of emotion. In emotional epilepsy it is not the emotion itself which gives rise to the convulsive seizure, but the circulatory changes occurring in association with it. Jean Lépine (*Lyon méd.*, Dec. 22, 1912).

Epidemic and sporadic cerebro-spinal meningitis, insolation, scarlet fever, typhoid fever, and other kindred diseases, if attended with prolonged high temperature or toxemia, may lead to the development of epilepsy, the relationship being apparently one of cause and effect. A unique convulsion from any acciden-

tal cause may start the habit in a predisposed individual.

Disease of the heart or blood-vessels interfering with the circulation in the brain, and its nutrition, is properly regarded, we think, as a sufficient explanation of the etiology in certain cases of cardiac and so-called senile epilepsy, and perhaps in other obscure cases.

In the 3 principal varieties of epilepsy disturbances of the circulation are among the dominating features, the writer being led to conclude as follows: (1) Abnormalities of cardiovascular phenomena occur in the vast majority of epileptic seizures. (2) The grosser forms of cardiac disease rarely occur in epilepsy. In fact, they are present in so small a proportion as to indicate that they are accidental rather than determining factors of it. (3) That a cerebral disease or abnormality may produce epilepsy is well established. The evidence shows that removal of enlarged veins or nevoid growths adjacent to the base of the skull has been followed by cessation of the seizure. (4) There is therefore a reciprocal relation between circulatory disorders and epilepsy to this extent that epilepsy causes circulatory disturbances and that abnormalities of blood or vessels cause epilepsy. This reciprocal relation he believes to have been hitherto overlooked. (5) In most forms of epilepsy there is cerebral anemia, and this is relieved effectively by various **heart stimulants**, the **high-frequency current**, and **radiant electric light**. The importance of the use of cardiac stimulants in epilepsy has not been properly appreciated by the profession. T. E. Satterthwaite (*N. Y. Med. Jour.*, Nov. 11, 1916).

Insofar as concerns the organic and toxic epilepsies, the etiology and pathology are those of the primary organic disease, the epilepsy in such cases appearing in the individual only as a single, though sometimes the most

important, symptom. Any source of irritation within the cranial cavity, whether chemical or mechanical, may—though it by no means must—induce a convulsion.

In the course of a prolonged and persistent asystole the alterations in the circulation of blood in the brain, the presence of toxic substances, and the vascular and inflammatory lesions in the brain combine to produce a hyperexcitability of the latter organ. This may express itself in crises of true epilepsy or of related psychic manifestations. F. Monisset and J. Gate (*Revue de méd.; Med. Record*, Sept. 7, 1921).

Of interest in connection with the subject of general predisposition to epilepsy are the statements of Peterson that the disease bears a ratio to the general population in this country of 1 to 500, and the further statement by Gray that a considerable majority of all epileptics have dark hair and eyes.

Reflex epilepsy, the existence of which is somewhat widely questioned, quite probably occurs, but in comparatively rare instances. Among the innumerable conditions of peripheral disease which have been noted as bearing an apparently causative relationship to the development of epilepsy are phimosis, adherent prepuce or clitoris, stenosis of the uterine os, nerve-cicatrices or surgical disease of the limbs or joints implicating nerve-trunks, carious teeth, eye-strain (esophoria, exophoria), obstructive disease of the nasal passages, aural diseases, etc.

Spratling's work on "Epilepsy and its Treatment" testifies unintentionally to the potent influence of eye-strain. If only 1 in 100 epileptics can be cured by relieving measures for eye-strain it would practically double

the number of cures of epilepsy. The writer reports 4 cases in which fits appeared to be entirely suppressed for considerable periods by the correction of optical defects. H. O. Reik (*Jour. Amer. Med. Assoc.*, May 4, 1907).

At the Massachusetts Hospital for Epileptics, the writers placed on full mydriasis 88 patients to eliminate eye-strain and keep them with paralyzed accommodation for one month. They then compared the results as evidenced by the number of seizures with the number shown in other months. The following results were obtained: The total number of seizures in a minimum month was 545, or an average of 6.1 per patient. The total number of seizures shown in a maximum month with the same patients was 1630, or an average of 19.6 per patient. Adding the totals, this gives 2275 seizures, which, divided and averaged, give 13.2 per patient. The results as regards the seizures during the month of full mydriasis was 1110, giving an average of 12.6 seizures per patient, or approximately the same as that afforded by averaging the maximum and minimum months. While admitting that eye-strain may be an excitant in an individual of sufficiently unstable nervous system, the writers believe that the rôle played by ocular defects in the causation of epilepsy is very slight. Hodskins and Moore (*Vt. Med. Monthly*, March, 1908).

Case in which one month after correction of eye-strain, December, although the number of severe convulsive seizures increased somewhat, the total number fell from 404 to 157. In January the total number fell to 85, and in February to 7. At the present writing, 6 months have passed with but 2 or 3 slightest *petit mal*, hardly noticeable symptoms. G. M. Gould (*Buffalo Med. Jour.*, May, 1908).

Case of a young man aged 23 who was subject to attacks resembling epilepsy, aggravated by the use of his eyes, which first appeared about

a year and a half before he was seen by the physician. Correction of the eye defect immediately was followed by cessation of the attacks, and he has been free from them for two and a half years. J. S. Wyler (Jour. Amer. Med. Assoc., June 8, 1912).

There is much to support the reflex theory in both experimental and clinical experience, although, as with many other phases of the subject, it is, as yet, no more than a theory.

Eight cases in which the epilepsy was due to reflex action from adenoid vegetations, their removal putting an end to the tendency. J. Tornai (Wiener klin. Woch., Oct. 3, 1912).

A study of 210 cases led the writer to conclude that since symptomatic and idiopathic cases are similar as regards age curve, constipation, sella turcica pathology and possibly lowered basal metabolism, the symptomatic cases can be regarded as potential epileptics in which the epileptic seizures have merely been waiting an exciting cause to manifest themselves. Nielsen (Med. Jour. and Record, Sept. 16, 1925).

Constipation being often observed, C. A. L. Reed attributed the seizures to a specific organism, the *Bacillus epilepticus*, found mainly in the cecum. His findings were supported by Terhune, but not by others.

**PATHOLOGY.**—The true pathology of idiopathic epilepsy is as yet an unwritten chapter in the history of the disease. We have reason to believe that the essential location of the conditions causative of the explosions which constitute epilepsy is in some part of the brain cortex. The theory of interference with inhibition through irritation of the higher cells of the cortex, a theory elaborated *in extenso* by Hughlings-Jackson, is generally accepted, but not yet proved. This theory is not inconsistent with the

experimental conclusions of Nothnagel, tending to show the existence of a lower convulsive center in the floor of the fourth ventricle (pons).

Dilatation of the lateral ventricle was found in 75 epileptics examined post mortem. Of these 57 presented gross brain lesions; 31 presented cortical lesions as well as dilated ventricles; 16, lesions of the cortex alone, while 14, with normal appearing cortex, showed dilated lateral ventricles. In the 43 brains presenting cortical lesions, the posterior portion of the brain was by far the most frequently affected, especially the occipital lobes. The convolutional shrinkage in this region was often marked in the brains. Next in order of frequency was the general cerebral gliosis, where the entire cerebellum appeared to be involved. Softenings were noted only 6 times, once being general and 5 times focalized. In only 2 cases of the 75 was there evidence of arterial rupture. Gliosis and atrophy of one hemisphere alone were noted in 8 cases of the 41 with dilated ventricle; 27 brains presented abnormalities of the cortex; in 14 instances the cortex was not grossly abnormal but the ventricular dilatation was of such a degree as to leave no doubt of its abnormality. Thoma (Jour. Mental and Nerv. Dis., Jan., 1920).

The study of the morbid anatomy of epilepsy has so far been equally inconclusive. The abnormal conditions noted have varied with different observers, even with the vastly improved laboratory technique employed within recent years. The tuberous or hypertrophic sclerosis, found chiefly upon the convexity of the convolutions by Barthez and Rilliet; the "gliosis" invading the normal cellular tissue, as described by Chaslin; the vacuolation of cortical cells with increase of spider-cells, found by Bevan Lewis; the hyperplasia of neuroglial tissue, with re-

duction in size and deformity of the cells, as observed by von Geison; these are all interesting and perhaps important; but numerous and insurmountable objections exist in each instance to their final acceptance.

The writer carried out macroscopic and microscopic examinations of 20 brains of epileptic patients who had died in an insane asylum. The one outstanding pathological fact was that in epilepsy there was marked destruction of cortical nerve-cells and an overgrowth of neuroglia. The writer's own cases showed macroscopically an occasional gross lesion such as a cyst, a definable sclerosed area, etc. He found the sclerosis most marked in the hippocampus in 15 per cent. of his cases. Microscopically, he found a chronic atrophic condition of the nerve-cells preceded by chromatolysis. He saw no evidence of phagocytosis of the nerve-cells by leucocytes. As regards the nerve-fibers, he found them in much greater abundance in sections treated by Cajal's method than in those treated by Pal's method, showing that the myelin sheath disappears before the axone. The changes in the neuroglia did not especially affect the outer layer of the cortex, as has been asserted. All the changes were more marked according as the case was one suffering from a large number of fits or not. Changes in the vessels were not marked; small hemorrhages were seen in cases with severe fits. In older cases the vessels were dilated. The writer is unable to affirm that there is any special histopathological picture characteristic of epilepsy, but he considers epilepsy to be especially a disease of the cortex, having found only minor changes in the cerebellum, basal ganglia, medulla, and cervical ganglia. DeBuck (*Le Névrose*, June, 1907).

Alzheimer found acute and chronic changes in 60 per cent. of all cases examined. In the nerve-cells the changes vary from slight degrees of

chromatolysis to advanced atrophic degeneration. The extent of the change would seem to depend largely, if not entirely, upon the mode of death. Certain nerve-cells, showing well-marked excentration of the nucleus, which is usually of a globose character, are regarded as being typical of low-grade brains and to represent an embryonic type of nerve-cell. The vascular changes consist of dilatation and atrophy of the blood-vessel walls, perivascular infiltrations, and punctiform hemorrhages. The lymph-spaces are dilated and contain a foam-like exudate. Hyaline spheres or lobulated bodies are seen lying free in the lumen of the smaller vessels and capillaries, and sometimes large hyaline masses form casts of the vessels in which they lie. In neuroglia there is an increase of the glial tissue, especially that situated in the outer layers of the cortex, and of the cornu Ammonis. The meninges generally show slight fibroid thickening and a moderate leucocyte infiltration. Rupture of the vessels with extravasation of red blood-corpuscles and a delicate unorganized foam-like exudate are always present. The lesions found in the brains of epileptics are of wide distribution. The cerebellar membranes are often more affected than the cerebral. The glial changes are distributed unevenly over the whole surface of the cerebrum, but some regions are more especially involved—viz., the frontal and occipital regions, the cornu Ammonis, and the gyri around the fissure of Rolando. It is now generally accepted that such changes are the effects, and not the cause, of the seizures. Turner (*Lancet*, July 16, 1910).

Our knowledge as to the pathogeny of epilepsy is scarcely less obscure and no more satisfactory. Anemia or hyperemia in extreme degree may, either of them, excite a convulsion. This is a fact of experimental demonstration as well as of common clinical experience.

Mechanical irritation—as from trauma, neoplasm, or foreign bodies—is an agency capable of inducing convulsive attacks, as is well known.

Transmitted irritation from the periphery, through the medium of some local condition of disease,—as, for example, an injured nerve,—may excite a convulsive explosion of the corresponding cortical center. Carious teeth, stenosis of the uterine os, volvulus of the intestine, adherent prepuce, and many other conditions of local disease may, through the medium of transmitted irritation along the afferent nerve-trunks provoke an explosion of the related cells of the cortex. Such cases constitute the much-questioned, but undeniably existent, class of reflex epilepsies. Finally, we have as a factor in the pathogenesis of epilepsy certain states of toxemia, some of them autogenous in origin, others depending upon the introduction from external sources of poisons with a relative affinity for the cortex.

The toxic epilepsies—those which are as yet positively determinable as such—are not numerous. There is reason to believe, however, that much more information remains to be gained as to the true pathogeny of epilepsy from the crucible and the chemist than from the scalpel and the anatomist.

The metabolic findings in epileptics indicate that the disease is of toxic origin in some cases, the brain being peculiarly sensitive to certain metabolic disturbances. Kauffmann (Münch. med. Woch., Nov. 10, 1908).

In a study of 775 necropsy protocols of patients in a general hospital, the incidence of intestinal adhesions and peritoneal bands was found to be relatively the same (18.3 per cent.) as in a series of 280 necropsies on epi-

leptics. Hence the writer believes that the constipation of epileptics, to which a toxemia has been attributed, cannot be said to be due to factors differing from those usually considered in the colonic stasis of other patients. Caro (Boston Med. and Surg. Jour., Aug. 16, 1917).

The writer found, as a seizure impends, an increase in the blood and urine of substances giving an alkaline reaction. During the seizure and afterward there is a pronounced turn to an acid reaction. All the testimony to date indicates that the composition of the urine undergoes certain abnormal changes by which the degree of acidity is materially altered. Bisgaard (Hospitalstidende, July 17, 1918).

In all of 27 cases studied by the writer the clinical and laboratory evidence pointed to chronic intestinal stasis and intestinal catarrh as prominent causes. A. W. Robertson (Brit. Med. Jour., Dec. 27, 1924).

One of the most interesting phases of that most fascinating field of newer pathology,—perverted internal secretions,—and one which holds, I believe, great promise in the direction of enlightenment as to the pathogenesis of epilepsy, is today attracting much attention and experimental study. The thyroid, the pituitary, and the suprarenals are all being charged with etiological responsibility, through perversion of function, individually or collectively. Nothing approaching a *quod erat demonstrandum* has yet been attained, but I am one of those who believe that it is in this field of research that we shall find the answer to many of the hitherto unsolved mysteries of this, one of the oldest-known diseases in the annals of medicine.

The dominant feature in the pathogenesis of the convulsions is impairment of metabolism, the spasmogenic agent being some toxic



agent in the blood-stream. Pathological variations of vasomotor action, due more or less to a morbid condition of the blood, have also asserted themselves so strikingly in the production of fits that some observers have been inclined to regard them as the foundation of the whole symptom-complex. Again, destruction of the spasmogenic agent has been urged by some as the only reasonable principle of cure in opposition to the use of bromides and chloral, which tend to increase its formation in the blood-stream. In a large proportion of cases the accumulation of these wastes is due to insufficiency of certain ductless glands, particularly the adrenals and thyroid. These organs, according to the writer, play an important rôle in the conversion of toxic wastes into benign and eliminable end products. Hence the beneficial influence of thyroid preparations in suitable cases. C. E. de M. Sajous (Monthly Cyclo. of Pract. Med., March and April, 1907).

The two predominating lines of advance in recent years are: The hereditariness of the disease, and disorders of metabolism due to perversion of the internal secretions of the ductless glands. Genuine epilepsy seems to be dependent upon certain unknown complex hereditary factors which bring about a form of cortical and subcortical instability. Upon this a variety of endogenous toxins may act to cause the disease. The fit is a manifestation of a reflex action of the disease, and as such should not be seriously interfered with by sedatives *per se*. As long as there is hope of bringing the real clinical pathogenesis under control, the use of sedatives is to be thoroughly discouraged. L. Pierce Clark (N. Y. State Jour. of Med., July, 1912).

True epilepsy, representing about 35 per cent. of all forms, according to the writer, is due to a toxemia by normal food and cell products, developed when these fail to be sufficiently neutralized by the action of the thyroid and parathyroid glands which normally serve to protect the central

nervous system against toxins. The glandular insufficiency may be due to some disorder of the sympathetic system, but the cortical lesions are secondary to the chronic intoxication. Injections of freshly expressed beef **thyroid and parathyroid juice** caused a complete disappearance of the symptoms. Bolten (Nederlandsch Tijdsch. v. Geneesk., June 28, 1913).

The writers conclude that at least 1 type of epilepsy is probably dependent upon absorption of toxic or poisonous products from the intestinal canal. This stasis may be produced by an overaction of the suprarenal gland. Hyperactivity of the adrenal gland may be caused by dysfunction of the pituitary or pancreas, irritation of the duodenum, or severe fright or emotional disturbance. Cotton, Corson-White and Stevenson (N. Y. Med. Jour., Sept. 16, 1916).

The writer divides epilepsy cases into 2 groups, those due to brain lesions and those due to the endocrins. The thyroid and parathyroids may be responsible for the disease directly or indirectly, but in the cerebral group the primary cause may be infectious, toxic, traumatic, or from physical malformation or tumor growth. Bambaren (Anales de la Fac. de Med., Lima, May-June, 1920).

In 90 cases examined by the writer by X-ray to ascertain the possibility of *pituitary lesions*, there were found: Tumors or evidence of pressure in the interpituitary area, 9 cases; bony deposits, 52 cases; small areas, 10 cases; calcareous degeneration, 2 cases; cerebropathy (not shown by the X-ray), 9 cases; no changes, 8 cases. In 24 cases in persons over 35 years of age, the knowledge of over 50 per cent. as being due to an organic insufficiency of the gland would be a strong argument to the effect that the other cases must have inefficient pituitary glands. A roentgenogram made again in 1 or more years showed, in some instances, no evidence of progression. If the cases were due to struma or other tumor growths the process of enlargement had ceased. The writer found

extract of the whole **pituitary gland**, 2 grains (0.13 Gm.) 3 times a day, 4 hours after meals, the most satisfactory treatment. **Bromides** should be given simultaneously. McKennan (Arch. of Neurol. and Psych., Sept., 1920).

**PROGNOSIS.**—The prognosis in epilepsy may be said to be progressively bad in a direct ratio with the number of attacks or the duration of the disease in the patient affected. If of long standing, the prognosis is bad, regardless of the cause. One convulsion, even though it be accidental, invites another, and, if repeated a few times, the convulsive habit is established and is curable only in rare instances.

Even severe and long-standing cases of idiopathic epilepsy are susceptible of arrest or cure. The majority of the permanent cures without drugs show a gradual subsidence of seizures instead of abrupt cessation. In patients treated with sedatives the criterion of cure must be somewhat modified, as a period of several months or even a year may be required for complete elimination of the drugs from the system.

The bromides do not aid the prognosis in epilepsy, especially as regards permanent cures. The writer has seen many cases treated with them steadily advance in physical, mental, and moral deterioration notwithstanding cessation of seizures. He uses bromides only, 1, as a therapeutic means of determining the severity of the disease, by ascertaining the sedative level necessary to hold the fits in check; 2, as adjuvants after all discoverable causes are set right and in such cases as need some small degree of sedation to bridge over certain periods. The seizures should no longer usurp the whole field of attention with their special therapy of sedation.

Fully two-thirds of all the patients with "idiopathic" epilepsy show some

functional anomaly of metabolism, either congenital or acquired; hence diet holds first place in the hygienic treatment. L. Pierce Clark (Arch. of Intern. Med., Jan., 1912).

Organic epilepsy dependent upon focal disease of even circumscribed limits is no exception to this rule, unless recognized promptly and treated properly by surgical procedure at once. Epilepsy due to syphilis, if promptly treated, can be cured; if treatment is delayed, it quickly becomes as intractable as any other form of the disease. This is true also of the toxic and reflex varieties. The element of heredity is of sinister significance in proportion to the intensity with which it may appear in the individual family history.

The age of onset is of importance, both as regards the curability of the disease and the development of serious complications. In epilepsy beginning in early childhood the tendency to the development of *status epilepticus*, a condition dangerous to life, is increased. I have seen this condition in 17 cases and in every one of them the disease began before the age of 10 years. The development of dementia is more probable the earlier the onset of epilepsy. Mania as a complication is more likely to be found in cases developing at puberty or later in life.

Epilepsy that is observed to develop without assignable cause at middle age (the *épilepsie tardive* of Forel) seems more amenable to treatment and the prognosis is rather better. In one such case, however, observed by the writer, the disease having developed after the age of 30, there being a history of parental syphilis, the patient died in an epileptic attack, the

disease having persisted for several years.

Histories of 7 boys who all presented what seemed to be typical epilepsy and yet, after a time, improvement ensued so that a year or two to date has elapsed without further symptoms, although previously the seizures had been frequent. Even if the cure is not complete and permanent, yet this intermission of a year or so is a great gain for the mental development of the child. During the years the children were under observation there was nothing to shake the diagnosis of epilepsy. The patients are now from 9 to 18 years old. In another case a boy of 7 had two typical seiures with foam at the mouth, etc. He was vigorously purged and an ascaris was passed; during the two years since there has been nothing to suggest a tendency to epilepsy. Another boy of 5 has had no seizures for three years to date, although before that he had had convulsions several times a day after the age of 18 months; tetany had been diagnosed in this case. In another case a little girl had numerous attacks of sudden blank staring, dizziness, etc., with pavor nocturnus, suggesting a tendency to epilepsy, but these attacks gradually grew less frequent and there has been none for the last two years. The child is now 6 and is rather backward in school, but otherwise apparently normal. In 3 other cases the writer found that apparently typical epileptic seizures were the first manifestations of a severe progressive brain or meningeal disease; later the seizures gradually ceased. He believes that these 13 personal experiences of his justify the conclusion that the prognosis of epilepsy in children need not be inevitably unfavorable. Zappert (Jour. Amer. Med. Assoc., from Med. Klinik, Feb. 11, 1912).

Death from or during an epileptic seizure is not uncommon. The *status epilepticus* is especially dangerous to life. Paralysis of the cardiac or

respiratory center is usually the immediate cause. Mechanical asphyxia is not infrequent. No reputable life-insurance company will accept an applicant known to be affected with epilepsy.

Death is imminent at the time of seizures, unless help is at hand. The cause may be traumatic, suffocation may take place, or death may occur without any apparent cause. Epileptics dying in a seizure will usually show some, but rarely if ever all, of the signs of seizure. The anatomical findings are edema and congestion, and often the diagnosis of seizure death has to be made largely by exclusion. It follows that the epileptic should be left by himself as little as possible. His walks should be in company or else in frequented places, and his repose should be under the watchful eye of a night nurse, or at least he should be in the same room with several other patients. J. F. Munson (Med. Record, Jan. 8, 1910).

The writer has collected 15 cases of sudden death during an epileptic fit, 13 from the writings of others, and 2 of his own experience; of these, 8 were due to cerebral lesions, bulbar hemorrhage twice, ventricular hemorrhage once, meningeal hemorrhage once, subpial hemorrhage twice, and cerebral congestion twice. (Of the non-cerebral causes, he gives rupture of heart three times (left ventricle twice, right ventricle once), rupture of aorta twice, obstruction of respiratory apparatus by food twice. In the author's 2 cases (bulbar hemorrhage and subpial hemorrhage) the ruptured vessels were healthy. M. A. Collins (Alienist and Neurologist, Nov., 1911).

What constitutes a cure in epilepsy? Freedom from attacks for one, two, five, or even ten years cannot be considered as final evidence of cure, since it has been the personal experience of every neurologist to note recurrences after such intervals of remission. I

have known a patient to exhibit a spontaneous remission for twenty-one years, the attack recurring without determinable new cause, and in exactly the same form, clinically, as at first. G. M. Hammond takes the position that relief from attacks for one or two years constitutes a cure, subsequent recurrences to be considered as new attacks. The objection to this teaching—there are many—is that, in some patients in whom the disease lasts through life, the attacks may be separated by intervals of a year or longer throughout the disease. Personally, I do not believe in the radical cure of epilepsy, if the disease has persisted for more than two years, except, perhaps, under an ideal environment attainable only in specially equipped institutions.

The duration of life after the onset of the disease may be several years, but as the onset is very common in the early years of life, the net result is the premature death of epileptics as compared with normal people. The causes of death in epileptics are quite largely associated with the disease itself, and may be divided into two main groups, pulmonary conditions and conditions of purely epileptic character. Pulmonary conditions usually have at their foundation the pulmonary edema which is so often associated with seizures, etc., and hence are secondary to the epilepsy. Exposure while helpless or automatic after a seizure may be responsible for lung conditions. It is possible that the frequent congestions and edemas occurring in these lungs make the soil fertile for the tubercle bacillus. Munson (Med. Record, Jan. 8, 1910).

Of importance in estimating the prognosis is the presence or absence of stigmata of degeneration. Epileptics exhibiting cranial asymmetry or

anomalies of development or well-marked intellectual or moral perversions are notoriously patients admitting only the most pessimistic prognosis. Well-marked periodicity in the occurrence of attacks in a subject constitutes a factor somewhat favorably modifying the prognosis.

**MEDICAL TREATMENT.**—The ideal treatment of idiopathic epilepsy is, in my opinion, attainable practically only through **institution environment**, organized on the colony plan, or as it is in Ohio or at Sonyea, New York.

The necessary regulation of the patient's habits, diet, clothing, exercise, sleep, and the employment of various adjuncts, direct and indirect, such as hydrotherapy and gymnastics, and appropriate culture of the mind and morals, can be accomplished systematically only in an institution established and conducted for such a purpose.

Where this is impossible, some such general plan as the following is advisable: Epileptics should be given some employment always, preferably physical and congenial and out-of-doors.

The **diet** should be regulated to two meals a day. Plain, wholesome food simply and properly cooked should be given liberally, but not in excess. Epileptics should be trained to eat slowly and to thoroughly masticate all food.

Of 17 cases, 10 were entirely freed from convulsions and 4 markedly improved by a **diet** consisting of only 10 to 15 Gm. of carbohydrate a day, with not over 1 Gm. of protein per kilo. of weight, and enough fat to make up calories. The best results were obtained in *petit mal*. Peterman (Amer. Jour. Dis. of Childr., July, 1924).

The writer places his patients under a system of intensive training and dietetic regimen supervised by a "nurse-trainer" who lives with the patient on the same schedule and draws up daily detailed reports of his condition. The measures outlined for these cases include a **diet** consisting chiefly of cooked cereals, stewed fruit, milk, eggs, fish, and vegetables; calisthenic **exercises**, and a walk in the morning; periods of rest morning and afternoon; wood sawing or other useful occupation; **warm bath** and general **massage** in the evening; high **colon irrigations** every other night until colitis is reduced; **castor oil** or **calomel** every ten days. A daily uranalysis is made. Nearly every case with metabolic defect shows either indican or albumin for the first two or three months, later disappearing.

All patients were found by the writer to benefit more or less permanently by this plan of treatment. L. Pierce Clark (Archives of Internal Medicine, Jan., 1912).

The toxics responsible for the paroxysms are the result of an incapacity to metabolize an amount of protein which the average individual can take with impunity. The most important feature of correct management is **limitation of the proteins**. Tom A. Williams (Med. Rec., May 8, 1915).

Very little fluid should be allowed with meals. No special constant diet table is either necessary or advisable, except in individual patients in whom some special indication exists. The two meals should be given at 10 A.M. and 5 P.M. The patient should be required to drink water freely and at regular intervals between meals—as much as 3 or 4 pints to be taken daily.

Some years ago, H. R. Geyelin introduced a **fasting method**, food being withdrawn suddenly and the patient given distilled water in excess at first, then thin broths. Short fasts

from 3 to 10 days were thus borne without discomfort. The value of the method, however, is still to be shown.

The starvation treatment is effective only while it is continued and while the patient remains in bed. The water treatment may be useful in those epileptics who have series of attacks at certain long intervals; these patients may be starved every 2 or 3 months for 10 or 12 days. A. Goldbloom (Can. Med. Assoc. Jour., Aug., 1922).

In 13 cases, mostly severe, 2 to 6 days of **fasting** resulted in temporary suspension of the seizures and mental improvement, in several instances persisting for some time. Schou and Teglbjærg (Hospitalstid., Jan. 22, 1925).

A few fair results were obtained in the epilepsy of children by **starvation**. The writer reserves this treatment for cases of impending status epilepticus. An **acidotic diet** (meat, cream, eggs) was also effectual in a few instances. When he added a little sugar to the water allowed to the fasting children, the acetoneuria disappeared and the seizures returned. Karger (Klin. Woch., Mar. 19, 1926).

The living rooms should be light and never overheated or contaminated by impure air, *i.e.*, well ventilated. Epileptics should be carefully protected from exposure to extremes of temperature. **Tonic baths** at proper intervals, keeping the skin active, and assisting in general nutrition, are valuable, but there is no special system of hydrotherapy which will cure cases of epilepsy.

As regards the drug treatment, we are still dependent upon the **bromides**. With regard to the use of the bromides in epilepsy I am firmly of the belief that the **curse of the epileptic** was the discovery that the bromine salts palliated and modified the disease. I have never seen a case of epi-

lepsy cured by the bromides, and I do not believe that the theory of its use permits such a result. It modifies; it palliates; but it does not cure. The mode of using bromides is given below.

Antitoxins and various other sensational specifics, including hypnotism, have been vaunted in recent years, but have failed to stand the tests of trial fairly made.

As I have indicated under pathology, a field of experimental **organotherapy** in epilepsy has lately developed, which invites attention. Nothing of positive demonstrated curative value has been established, but a rational basis for such experimentation has been laid, and much of promise appears as possible in this direction. The negative argument alone of abject helplessness in curative resources is in itself sufficient defense for this new departure.

The various ductless glands have been used extensively in this disease but on lines in keeping with the empirical methods fostered by the prevailing ignorance of the subject as a whole. Despite this fact, organotherapy has proven valuable whenever the agents given happened to strike the right note of a case—an indication that when the profession will cease following the misleading influence of physiologists, rational organotherapy will prove of great value in this disease.

In previous issues of this work and in the article on ANIMAL EXTRACTS the value of **thyroid gland** in certain cases has been summarized. Besides this agent, **pancreatic extracts** and the following have been used by many. A few are enumerated below in their chronological order. Jelliffe (N. Y. Med. Jour., Dec. 4, 1920) found **parathyroid extract** useful, particularly when given by rectum in its crude state. Lowenstein (Amer. Jour. Med. Sci., Jan, 1922) studied 16 cases for symptoms traceable to the pituitary. Five showed 1 or more features possibly ascribable to pituitary changes; 6 gave abnormal mental reactions, and 8 showed under X-ray exami-

nation changes in the sella turcica. But 3 of the latter, however, improved under pituitary treatment. **Pituitary** (pituitrin or whole gland) improved 5 of the cases, the best results being obtained when it was given hypodermically. One-half c.c. once or twice weekly sufficed. None of the cases with "typical epileptic constitution," or those with abnormalities of the fundi or visual fields, were improved. Leahy (N. Y. State Jour. Med., Jan., 1922) had 7 cases showing, in practically every instance, in addition to polyglandular involvement, some direct connection with ovarian deficiency. One severe case yielded to **corpus luteum** given several months, the seizures, initiated by vertigo, having occurred preceding menstruation. In a second case, in which menstruation had been defective and scanty, the seizures being nocturnal and accompanied by mental phenomena, great benefit was obtained from **ovarian substance**, 5 grains (0.3 Gm.) *t. i. d.* before meals. A third case, with somewhat similar symptoms and a sella of small size, also improved under **pituitary gland**, both anterior and posterior, 1 grain (0.065 Gm.) *t. i. d.* before meals. A case of **hystero-epilepsy**, with delayed puberty, observed by T. C. Graves (Lancet, Dec. 4, 1920), was successfully treated with **testicular extract**. He refers to 2 observers who also noted a diminished intensity of the symptoms under 1 tablet and non-recurrence under 2 tablets. According to R. H. Spangler (Atlantic Med. Jour., Dec., 1924), a certain proportion of the cases may be regarded as endocrin epilepsy. He favors non-specific protein injections in the form of **venom protein** (crotalin) for activation of the endocrins. **Gland substances** are also given by mouth. M. Kern (Hosp. Soc. Serv., May, 1924) reported gratifying results in 4 out of 5 cases from combined **thyroid, pituitary, ovarian and testicular extracts**. G. C. Bolten (Ned. Maand. v. Gen., xii, 637, 1924) reported a number of cases notably improved by **thyroid gland**. Bisgaard (Acta med. scand., Jan. 1, 1925) maintains that **parathyroid extract** is useful, restoring the ammonia values.—EDITORS.

The coal-tar derivatives—**antipyrin, phenacetin, lactophenin**, etc.—have also had their day, although their use

is not altogether without benefit temporarily under certain circumstances.

Ethylene bromide, amylene hydrate, sulphonal, trional, curare, and solanum Carolinense are a few among the hundreds of remedies recommended which have proved of only slight value or useless altogether, or, as with amylene hydrate and curare, worse than useless. **Borax**, sometimes designated as **biborate of sodium**, is an exception in that it rarely does seem to possess a positive value, especially in nocturnal epilepsy. The dose is from 15 to 60 grains (1 to 4 Gm.) once, twice, or three times daily. Very much larger doses have been given and have been well borne. In this variety of epilepsy, too, some hypnotics—**sulphonal**, **trional**, **chloralamide**, and **urethane**—have a useful purpose as occasional temporary substitutes for the bromides.

Treatment with **borax** has been introduced in France. The best results were obtained with the following combination: **Potassium bromide**, 15 grains (1 Gm.); **purified borax**,  $7\frac{1}{2}$  grains (0.5 Gm.), **Fowler's solution**, 2 minims (0.125 c.c.). This is given 3 times a day. The results witnessed were, marked general mental improvement; freedom from stupor after convulsions; disappearance of irritability and quarrelsome tendencies, and complete change of habits. J. McCartney (Brit. Med. Jour., Jan. 6, 1923).

In giving the bromides certain general facts should be recognized. The **potassium salt** is the most effective.

All **bromide salts** should be specially investigated as to purity of manufacture. Every dose of bromide should be given well diluted. The dose is inconstant necessarily and varies with the type and intensity of the disease in each patient. In an

ordinary case, with attacks of moderate severity occurring four or five times a month, or less often, the patient should begin with 20-grain (1.3 Gm.) doses twice daily. This may be increased or diminished according to the effect. An insufficient dosage is practically useless; on the other hand, no unnecessary excess of the drug should be continuously introduced into the system, since bromism, if prolonged, induces a condition scarcely less deplorable than epilepsy.

If the attacks occur at more or less regular intervals, as at the menstrual epoch in women, such periods of attack should be anticipated by temporarily increased doses. Gowers's plan is quite effective in some cases, though bordering on the heroic. He gave one full dose of **potassium bromide** in the morning after breakfast in half a pint of water (250 c.c.), beginning with 2 drams (8 Gm.) every second morning, increased to 3 drams (12 Gm.) every third morning, and 4 or more drams (16 Gm.)—an ounce (30 Gm.) sometimes—every fifth day. The dose and order of interval are then reversed and the treatment is continued in this way for six weeks; small doses are then given for a year or more.

It is desirable to give just that amount of **bromide** which, being **added grain by grain** on the return of attacks, will finally prevent their occurrence. Although the effects of bromide on the skin are annoying, they may generally be avoided if the person will bear full doses of **arsenic** and use **hot baths**. There is, however, a small percentage of persons who are so susceptible to the bad effects of these drugs that a dose of a dram a day will within a week produce large rupia-like ulcerations, which so strongly resemble the rupia of

syphilis that when the writer first saw and described them he was for a time completely deceived.

As you patiently add grain by grain to attain the restraining dose, so you must at the end of 2 years without attacks as slowly withdraw the drug grain by grain. Weir Mitchell (*Therap. Gaz.*, March, 1912).

**Potassium bromide** seems to be curiously limited in its power for good in the treatment of epilepsy. Occasionally, after having been effective for weeks or months or even years, its effectiveness will, without assignable cause, cease. This is true not only of potassium bromide, but of nearly, if not every, other drug useful in epilepsy. Some other one of the **bromides**, or several of them in combination (**sodium, strontium, ammonium, lithium**,—valuable in the order mentioned), or one or two of the bromides in solution with **antipyrin** or in combination with **phenacetin**, may be advantageously substituted for the continuous use of a single salt.

A diet low in salt, *i.e.*, poor in chlorine, has been found to increase the efficiency of the bromides, thus making it possible to administer smaller doses of the latter.

The beneficial effects of a diet which is arranged so as to be poor in chlorine, upon epileptic patients who are at the same time on the **bromide** treatment, were first urged by Toulouse and Richet. André Vitelman, in 1906, demonstrated that a rigid **dechlorinized diet** combined with the bromide treatment (2 Gm., or 30 grains, in 24 hours) in an epileptic caused the urea and the phosphates in the urine to be eliminated in much larger quantity. (*Journal des Praticiens*; *N. Y. Med. Jour.*, Aug. 17, 1907.)

Results in 15 cases of epilepsy treated by a diet low in salt in combination with the **bromide** treatment.

These patients were observed continuously for a period of five years, and the improvement has been constantly maintained. Immediate improvement followed the **withdrawal of sodium chloride from the diet**. In 6 cases the attacks ceased completely; in the other 9 there was marked improvement. Ulrich (*Münch. med. Woch.*, Bd. lix, S. 1947, 2007, 1912).

In a case observed by the writer, **skimmed milk and bread without butter** sufficed to nourish the child and prevent recurrence of seizures. DeLue (*Trans. Amer. Med. Assoc.*; *Med. Rec.*, June 11, 1921).

The hypnotic **luminal (phenobarbital)**, differing from veronal (**barbital**) only in that one ethyl group has been replaced by one phenyl group, has been widely substituted for the bromides. It does not cause the mental or confused state observed in cases taking the latter, and does not tend to habit formation, although the effects of its abuse may suggest alcoholism. There is a definite decrease in the number of seizures and the resulting injuries, while the patient becomes quieter and more amenable to treatment. Cumulative effects or paralyzes do not ensue. It favors menstrual function and may cause an increase in weight. Grand mal seizures tend to become converted into petit mal and then to cease for periods more or less prolonged. The drug is only valuable as a palliative, however, the seizures tending to return when it is stopped.

The dose for an adult is 1½ grains (0.1 Gm.) of luminal and 2 grains (0.13 Gm.) of luminal-sodium,—preferred by some authors, J. T. Fox (*Lancet*, Sept. 10, 1921), for instance,—given at bedtime. The effects may not be seen for a week or two, but are usually noted from the start. In



delayed cases a small dose of bromide of sodium will bring on the effects of luminal. In some the dose must be increased to perpetuate its effects. Other patients do not tolerate it well; in these, small doses should be tried along with a bromide salt. It should not be stopped abruptly, as the seizures may then recur with increased violence, and may even, as observed by Foley, initiate status epilepticus and thereby cause death.

Untoward effects occur in about 10 per cent. of cases treated with luminal. The patient may become irritable or complain of vertigo. An eruption resembling that of scarlet fever is sometimes observed, which disappears on stopping the drug. This is apt to occur when a renal disorder is also present. Zalla (*Riv. di patol. nerv.*, Apr. 4, 1921) administers **belladonna** and **hyoscyamus** besides the luminal to prevent excitement; he also recommends a **meatless diet** in this connection. Sajous has observed that any degree of constipation tends to promote the untoward effects of luminal, and that albumin in the urine, and casts, particularly, indicate the need of circumspection in its use.

The writer found that if he limited the administration of **luminal** to 1 dose at bedtime, these symptoms did not appear and the efficiency of the drug was not impaired and possibly was increased. It exerted a remarkable control over the seizures even in the most confirmed cases. The doses required were very small, a dose of  $1\frac{1}{2}$  grains (0.1 Gm.) of luminal or 2 grains (0.13 Gm.) of luminal-sodium given at bedtime being sufficient. He was rarely obliged to give as large a dose as 3 grains (0.2 Gm.). Dercum (*Therap. Gaz.*, Sept., 1919).

**Phenobarbital (luminal)** proves effective in idiopathic and traumatic epilepsy, but is of doubtful value in senile and syphilitic epilepsy. This drug and **bromides** may be combined and better results thus obtained in selected cases. Phenobarbital has a cumulative effect, which is corrected by a break of 2 days in each week. If the drug is suddenly broken off, the risk of a resulting series of seizures is much reduced by giving **bromides** at once. A safe dosage is  $1\frac{1}{2}$  grains (0.09 Gm.), given 5 days a week. Possible ill-effects, especially from larger doses, are a morbilliform or scarlatinoid rash, symptoms simulating alcoholic intoxication, severe diarrhea, mental hebetude, and delirium. Darling (*Arch. of Neurol. and Psych.*, Apr., 1923).

The writer prefers giving not over  $1\frac{1}{2}$  grains (0.09 Gm.) of **phenobarbital** in the morning in diurnal epilepsy, not over 25 grains (1.6 Gm.) of **bromide** at night in nocturnal epilepsy, and both remedies when attacks occur both day and night. J. Collier (*Lancet*, Aug. 23, 1924).

Sometimes the addition of one of the motor depressants—as **hyoscyamus**, **conium**, **belladonna**, or their alkaloids—is quite as effective, at least temporarily. As a matter of further curious interest it has been proved by experience that in such cases a change to almost any new drug will result in temporary improvement—a fact which explains, in part at least, the almost limitless pharmacopeia of the disease.

The use of opium, reintroduced, as is known, by Flechsig, is deserving of mention and a limited commendation. Flechsig's method consists in the daily administration of **opium** in the form of the solid extract in doses gradually increased up to several grains (12 to 15) daily, five or six weeks usually being required. Treatment by bromide is then substituted

for the **opium**. This treatment is of distinct benefit in old, long-standing, idiopathic epilepsies which have not been benefited by the bromides. It is contraindicated in recent epilepsies and in the organic cases.

**Chloretone** used in 12 obstinate cases and recommended where bromides fail. All cases showed marked reduction, and in 1 cessation, of attacks. It is best given in glycerin solution. In the robust 10 grains (0.65 Gm.) may be given *t. i. d.* Sometimes "chlorctonism" symptoms appear: Increasing dullness and drowsiness, later vertigo, irritability, pallor of mucous membranes, sluggish reflexes, albuminuria, and an eruption. The urine should be examined daily and the drug stopped if albuminuria or other symptoms appear. The benefit from chloretone usually persists a month after discontinuance. Bentley (Austral. Med. Gaz., March 20, 1911).

Four remedies are deserving of special mention in connection with special forms of epilepsy for the relief of which they seem especially efficacious: **Amyl nitrite** and **monobromated camphor** in cases of *petit mal*, **duboisine** in hysteroepilepsy, and **coniine hydrobromide** in the *status epilepticus*. Nitrite of amyl also possesses value as a drug which, if used promptly in cases preceded by an aura, will often prevent the further development of the attack. **Chloroform** by **inhalations** is at times temporarily useful in controlling the *status epilepticus*.

Clonic spasms can be suppressed and the consciousness restored by **placing the epileptic on his left side during the tonic period**. This method of arresting the seizure was first successful by McConaghey, of Edinburgh, and the author has found it successful in every instance in which it has been applied. Crocq (Fourteenth French Congress of Neurol.

and Psych.; Semaine méd., vol. xxiv, No. 32, 1904).

I have found the use of **cardiac tonics** of positive value in combination with the bromides in what is known as cardiac epilepsy. The condition of the heart and pulse is the guide to the selection of the adjuvant drug. **Sugar** has been advocated by some, though condemned by others.

The diet advocated by the writer is one **starch and sugar free**. He also gives **pancreatin** and **sodium bicarbonate** at meals, a dose of **Epsom salts** every fourth day, and **mineral oil** daily if needed. In only 2 cases did he give bromides, and then only for a short time. T. E. McMurray (N. Y. Med. Jour., Nov. 11, 1916).

The writer induced convulsions in rabbits, mice and dogs by injections of insulin, which caused hypoglycemia. He also noted an increase of epilepsy cases in Russia when sugar was scarce. Thereupon he tried **sugar** in epileptics with hypoglycemia. In 18 cases the seizures became rarer and milder; in 5 they appeared only once in from 4 to 6 months, while before the treatment they occurred every day in 1 patient, and 3 or 4 times in a month, in the others. Since blood with reduced sugar may irritate the nervous centers, causing convulsions, the administration of sugar should prevent them. From 50 to 100 Gm. (1½ to 3½ ounces) of **glucose**, dissolved in water, with lemon juice, or 200 Gm. (6½ ounces) of sugar, was given daily by the mouth. The amount of sugar was reduced to 5-25 Gm. (1¼-6¼ drams) when sweet fruits or syrups were being taken. Wladyciko (Presse méd., Nov. 7, 1925).

To a certain extent, though far more limited than one would suppose from *a priori* reasoning, the etiology affords a basis for treatment. **Anti-syphilitic treatment** should be at least given an energetic trial, as epilepsy is due primarily to syphilis. Such patients, however, as a matter of fact,

are not often cured by this means, and as a further fact of interest it will be found that such patients do not bear well energetic specific treatment. Various toxic agencies or conditions of visceral disease, standing in a presumably causative relationship, should be treated, of course, but cure of the toxemia or the visceral disease rarely results in cure of epilepsy.

Yet the possibility of autointoxication of intestinal origin should invariably be looked upon as a possible cause. Sajous has treated 2 cases in which elimination of this factor proved curative. One of the cases has been well 15 years, and has borne children without eclampsia; yet it was virtually one of status epilepticus, the seizures occurring from 20 to 30 times every night. In the second case, the child, a boy of 8 years who has been well over 2 years, the seizures occurred 2 or 3 times a night and were inducing idiocy. **Free lavage** of the intestine, with postural changes to cause the fluid to bathe the cecum, and small doses of **thyroid gland** internally, besides **abstention from proteins**, were the measures employed.—EDITORS.

**Veronal** in small doses is often a more efficient drug than the bromides. The writer gives it during the intermissions in doses of 0.1 to 0.3 Gm. (1½ to 5 grains) from twice a day to twice a week, depending upon the age and the severity of the case. A cumulative effect or intoxication was not observed. Liebl (Med. Klin., Nu. 45, 1909).

Having operated on a young epileptic for inguinal hernia under **spinal anesthesia**, the writer learned, 2 years later, that the young man had had no seizures, although previously they had recurred every 10 or 15 days for 9 years. Systematic use of spinal anesthesia in epileptics thereafter uniformly yielded great improvement. Giacomelli (Gaz. degli osped., Jan. 18, 1912).

(1) Secure bowel movements once or twice daily. (2) Have patient drink **water** freely. (3) Tepid **sponge bathing** or brief immersion **baths** fol-

lowed by gentle rubbing. (4) **Mild exercise in open air**. (5) **Mixed diet**, consisting of vegetables and milk in liberal amount, and also white meats; starchy foods in limited quantity; normal amount of fats. Correct digestive difficulties. (6) **Bromides** to be used early in disease and in sufficient amount to control seizures. (7) **Sodium chloride withdrawal** found an aid to bromides, though prohibition of salt should not be so radical as to cause anorexia and loss of weight. (8) Combination of **sodium glycerophosphate** with bromides proves beneficial. (9) **Thyroid extract** valuable in epileptic children with arrest of development, as well as, occasionally, in other cases; to be given persistently, in small doses; after a time, it will be found bromides can be reduced or even for a while suspended. (10) Trial of **pituitrin** in epilepsy justifiable. (11) Symptoms preliminary to seizures, such as headache, depression, etc., indicate the prophylactic use of a **saline purge**, **diminution of food**, and increased bromide dosage. Dercum (Therap. Gaz., March, 1912).

The writer observed 3 cases in young women, 1 of whom had her first epileptic seizure after severe tonsillitis and another after scarlet fever. These patients were given, in the course of 20 months to 2½ years, 8 to 12 series of intravenous injections of **neoarsphenamin**, each series totalling about 5 Gm. (1¼ drams) of the drug. The seizures, as a result of this treatment, have been absent for 11 months to 8 years. In 2 the Wassermann was negative and in the other doubtful. Injections of **sodium nucleinate**, **tuberculin**, or **blister fluid** were given in the intervals. Page (Presse méd., Sept. 9, 1922).

The frequently demonstrated fact that the coagulability of the blood is reduced in epilepsy suggested the use of calcium, the most satisfactory salt of which is **calcium lactate**. From 5 to 15 grains (0.3 to 1 Gm.) may be given three times daily.

The writer gave **calcium carbonate** twice daily in the form of a cachet containing 10 gr. (0.6 Gm.) and found it of real service. His experiments dealt with 5 epileptics, and extended over two years. The daily average of fits was considerably lessened while the salt was taken. A very great improvement occurred in the mental and physical conditions of the patients; and they were less confused, irritable, and excitable while taking the calcium carbonate. D. Linguerri (Bull. d. sci. méd., Dec., 1906).

The writer has successfully used **calcium lactate** in the treatment of epilepsy. All his patients have improved, some more so than others. The usual dose was 15 grains (1 Gm.) of calcium lactate three times a day. Littlejohn (Lancet, May 15, 1909).

In 29 cases of epilepsy **lime** had a pronounced effect in mitigating the seizures and reducing their number. The lime salts are preferable to the bromides at times, the best results being obtained when a course of lime was alternated with the ordinary bromide treatment. From 2 to 3 Gm. (30 to 45 grains) of **calcium hypophosphate** in fractional dose were given daily. The patients were all chronic epileptics, although the affection was of traumatic origin in some and associated with infantile spastic paralysis in others; the majority, however, were of the idiopathic variety. F. Ciccarelli (Policlinico, Feb. 7, 1909).

The official syrup of **calcium lactophosphate**, used in doses of from 1 to 2 drams (4 to 8 Gm.) 3 times a day, promotes sleep, decreases nervous irritability, and acts in some measure as an antidote to bromine acne. Bryant (Boston Med. and Surg. Jour., Oct. 7, 1915).

**Crotalin**, or rattlesnake venom, has recently been introduced, but without careful animal experimentation to determine its immediate or remote effects. The danger of anaphylaxis, pending such analytical work, renders

the use of this extremely toxic agent somewhat hazardous.

Series of 36 cases, between the ages of 5 and 62 years, were treated with **crotalin**. All were average cases. That form of the disease most influenced by the venom solution was the idiopathic or genuine epilepsy. The improvement in the mental condition of the patients was marked, while the frequency of epileptic attacks was greatly diminished. In regard to the dose, the writer recommends starting with  $\frac{1}{200}$  grain (0.0003 Gm.) and gradually increasing the strength according to the individual case. Patients vary greatly as to the swelling, erythema, and cellulitis produced by injection of the venom solution. The effect often varies, even in the same individual,  $\frac{1}{100}$  grain (0.0006 Gm.) sometimes causing more severe local reaction than  $\frac{1}{50}$  grain (0.001 Gm.). R. H. Spangler (N. Y. Med. Jour., Sept. 9, 1911).

The treatment of epilepsy with **crotalin**, i.e., the sterile, dilute virus of the rattlesnake. *Crotalus adamanteus*, was tried by the writer with very satisfactory results, although the time elapsed does not warrant a final judgment upon its value. Fachsenheim (Münch. med. Woch., Aug. 29, 1911).

The writer had a fatality from the use of crotalin. This shows that a sterile solution cannot be assured.

Welch and Ewing already in 1896 showed that rattlesnake venom destroys the bactericidal properties of the blood. The laboratory findings in the case reported left no reasonable doubt that the death was due to the presence in the crotalin solution of pathogenic bacteria. J. F. Anderson (Jour. Amer. Med. Assoc., Mar. 21, 1914).

**SURGICAL TREATMENT.**—**Intracranial surgery** is limited to those cases recognizable positively as dependent upon an organic lesion of limited extent and surgically accessible, the location of the explosive

focus being determinable at least approximately from the symptoms.

A series of 56 personal operations showed that it was justifiable: (a) In traumatic epilepsy with external evidence of injury; (b) *do.*, without evidence of injury when nature of attacks or symptoms immediately following injury indicates seat of lesion; (c) in Jacksonian epilepsy; (d) in general epilepsy where suggestion of a focal lesion may be found before or after attacks in some disturbance of motion, sensation, or reflexes. Gratifying results may be anticipated after operation in 10 to 25 per cent. of cases. Frazier (Therap. Gaz., March, 1912).

To the above class of cases may be added that small number included in the etiological variety known as reflex epilepsies. In organic epilepsies the results of surgical treatment depend upon the accuracy and promptness of diagnosis, including localization chiefly, and secondarily upon the promptness with which surgical interference is adopted, and the personal skill and surgical judgment of the operator. Shock and hemorrhage are practically the only immediate sources of danger, sepsis having eliminated other surgical complications. Both shock and hemorrhage are avoidable or can at least be reduced to a minimum which does not endanger life. Wyeth's method of accomplishing this result in intracranial operations by dividing the operation of entrance into two or more surgical *séances* upon succeeding days is eminently satisfactory. So safe, indeed, is this method as to have rendered perfectly legitimate surgical entrance of the skull for purely exploratory purposes.

**Surgical treatment** of epilepsy is indicated in cases which prove intractable to general medical and hygienic

treatment, and these, unless the disease be somehow arrested, will soon terminate in imbecility and death. In such cases the affected motor area is covered by more or less edema of the pia-arachnoid and this edema probably so affects the cells of the cortex as to predispose to or cause the epilepsy and imbecility. We can, by the operation of fenestration of the dura mater, drain these edematous areas and prevent reaccumulations. By the operation the progress of the disease has always been retarded in the 20 cases operated, while in several the fits ceased. Alexander (Lancet, Sept 30, 1911).

During the last ten years the writer has operated upon 106 cases of genuine generalized epilepsy after the method of Kocher, and investigation of all these cases has only recently been carried out. Of 58 cases on which operation was done upward of five years, 8 have been completely cured, 15 have been decidedly benefited, while 33 have not been benefited. Ito (Deut. Zeitsch. f. Chir., Bd. cxv, H. 5-6, 1912).

The technique of the operative procedure varies with each case appropriate for operation, as well as in accordance with the surgical peculiarities of the operator. There is a growing pessimism representing the return swing of the optimistic pendulum of ten years ago with regard to the value in results of surgical treatment for organic epilepsy. Von Bergmann and McCosh, among recent writers, unite in a demand for greater conservatism. Mason, quoted by Gray, tabulates 44 cases treated surgically, with 2 recoveries, or about 4½ per cent. This table is capable of another interpretation, however, which is decidedly more favorable from the fact that, in more than half the cases in which the time of observation after operation is said to have

been "insufficient to confirm the claim of cure," further lapse of time may serve to establish the claim at least in some of these cases.

**Exploratory trephining** is advised in traumatic epilepsy. In 11 cases operated by the writer—4 of idiopathic and 7 of surgical epilepsy,—cysts were found in 2 instances, cicatrices in 4, and edema of the pia in all. Improvement resulted in all the cases from removal of edematous fluid. The epileptic attacks returned in 4 cases. Tilmann (Munch. med. Woch., Nu. 32, 1909).

In the past there has been much ill-advised and indiscriminate operative intervention in the epilepsies, and some of the cases, viewed either from the purely surgical point of view or from the standpoint of the epileptologist, are sad commentaries on the ill-judged activity of the surgeon. The writer reports 19 cases in which some surgical intervention was undertaken on the head and which afterward came to autopsy. In some cases, the scar-tissue formation had been the evident cause of continued irritation and in others there was cerebral destruction which was sufficient to cause the attack, but in others there was apparently both a successful operation and an absence of lesion. The reason for this ill success is that there was a decided neuropathic taint in many of the family histories, which the operation does not remove. Again, some patients who desire operation have alcoholism or venereal excesses as part of their etiological equation. There again the knife is handicapped. In some of the traumatic cases the trauma is not the cause but is the result, of the first seizure, and therefore the operation fails to remove the original cause. Munson (N. Y. State Jour. of Med., Nov., 1912).

Of the total number of 3502 patients admitted to the Craig Colony for Epileptics, 48 had been trephined either before admission or during their treatment at the Colony. In a few of these the operation had been

repeated. Naturally none of the patients operated on at the Craig Colony had been trephined immediately after a trauma or the onset of the epilepsy, as they were all confirmed epileptics at the time of admission. The results of operation on these patients cannot be compared with those obtained by operation immediately after the trauma or in the early stages of the epilepsy. None of the patients trephined at the Colony have been permanently relieved from the attacks, although most of them were benefited, at least temporarily, by the operation. In several cases in which operation was done before admission, the condition of the patient had been made worse by the operation. Sharp (N. Y. State Jour. of Med., Nov., 1912).

The writer lays stress on focal infection, particularly in the intestinal tract, as the cause of epilepsy, and states that constipation is the most constant associated symptom. Visceral displacements, developed before the convulsions, exist in all cases. Intestinal infection is generally primary, but may be secondary to infection of the teeth, tonsils, or accessory sinuses. **Removal of all foci of infection** results in cure in patients in whom delay before operation has not resulted in secondary degenerative changes. C. A. L. Reed (Ky. Med. Jour., Sept., 1922).

A boy of 15 years had suffered from seizures beginning with peculiar sensations in the left lower jaw. The writers found an unerupted and impacted lower molar on each side, removal of which was followed by cessation of the seizures. W. G. and F. H. McGauley (Dental Cosmos, Jan., 1922).

Almost all cases of epilepsy which come within the etiological subtype "reflex" demand surgical measures of relief, the removal of the peripheral cause requiring, in most instances, the knife. Phimosis, cervical stenosis, carious teeth, nerve-cicatrices, diseases of the bones, eye-strain, and

ovarian disease are all conditions for which the knife or other surgical or mechanical agents are indicated.

In all cases of epilepsy, when such conditions or any one of them exist, either coincidently, alone, or as the presumable cause, they should be appropriately relieved. It will not always, nor indeed often, cure epilepsy; but such conditions undoubtedly aggravate the epileptic tendency, and should be eliminated. I have never yet seen a case of epilepsy cured or even benefited permanently by operations upon the eye-muscles or by removal of the ovaries, and I have seen scores of patients upon whom such operations have been done.

Such operations should be done, though with discrimination and always with the frank acknowledgment to the patient of the uncertainty of results.

In a case in a woman of 42, the writer witnessed recovery under **arsenic** and **X-ray** treatment. He ascribes the benefit to an influence on the endocrin functions. He also observed several cases of epilepsy connected with menstruation which were successfully treated with the **X-rays**. M. Fraenkel (Zent. f. Gyn., Sept. 13, 1924).

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### EPISTAXIS.—DEFINITION.—

Epistaxis is nasal hemorrhage, or bleeding from the interior of the nose. While the great majority of cases have their origin from some spot situated in the anterior part of the septum, the bleeding may take place from any portion of the mucous membrane.

The arterial supply of the interior of the nose is derived from the ophthalmic and the internal maxillary branches of the internal carotid artery, and from the superior coronary artery, which is a remote twig of the

external carotid. The ophthalmic artery divides into numerous branches, the anterior ethmoid accompanying the nasal nerve through the anterior ethmoid foramen and supplying the anterior ethmoid cells and frontal sinus, and also gives off other nasal branches, which are distributed similarly to those derived from the posterior ethmoid artery. The posterior ethmoid has its origin just as the ophthalmic artery approaches the inner wall of the orbit. It passes through the posterior foramen in the ethmoid bone, supplying the posterior ethmoid cells and giving off nasal branches which descend through the cribriform plate and spread over the upper and outer wall of the nose.

The internal maxillary gives off the nasopalatine, the infraorbital, and the alveolar arteries. The nasopalatine is the most important of these branches; it enters the nasal fossa at the posterior portion of the superior meatus, and divides into an internal and an external branch, the former passing obliquely downward and forward, supplying the mucous membrane covering the septum, and finally anastomosing with the descending palatine artery. The blood-supply to the nose proper from the infraorbital and the alveolar arteries is rather meager and pertains especially to the maxillary antrum.

The inferior artery of the septum is a branch of the superior coronary, and supplies the anterior portion of the septum; hence it is frequently held responsible for many cases of epistaxis from the so-called "hemorrhagic area" of the nose, or Kesselbach's spot, situated on the septum near the tip.

### ETIOLOGY.—1. *Traumatism*.—

One of the most frequent causes of bleeding from the nose is injury of some sort. A blow upon this organ produces a rupture of the smaller blood-vessels in the mucous membrane and permits a free flow of blood until checked. This may also result from violently blowing the nose. The pernicious habit of picking the nose is not infrequently the causative factor. Foreign bodies inhaled with the atmosphere and impinging against the vascular area, more directly exposed to such injury by an anterior devia-

tion of the septum, or their insertion by the patient, frequently predispose to hemorrhage. Postoperative bleeding is usually mild in degree and is seldom difficult to control. Bleeding from the nasal cavities following traumatism is particularly significant if fracture of the perpendicular plate of the ethmoid is determined, for this bone is usually involved in fractures of the anterior fossa of the skull. In such cases injury to the ophthalmic artery or its branches takes place.

2. *Diseases.*—Several diseases of a local nature may be responsible for bleeding from the nose. A catarrhal inflammation produces a chronic hyperemia of the mucous membrane, and the increased blood-supply resulting therefrom contributes to epistaxis. The veins in the anterior portion of the septum may be varicosed, or the effort to remove scabs, especially in atrophic rhinitis, may produce the same result. Adenoids in children, or a septal ulcer in a patient more advanced in years, is sometimes the contributing agency. One of the diagnostic signs of malignancy of the nasal chambers is the tendency for the tumor to bleed; however, some of the new growths of a benign nature may produce the same symptom, as has been noted in cases of nasal polypi. In the malignant growths especially, the hemorrhage takes place as the result of pressure necrosis or the active breaking-down process due to rapid development.

Many cases of nasal hemorrhage have occurred which have been traced directly to some constitutional disturbance. When the bleeding is from an apparently healthy nose some internal organ is probably at fault, in which case it may be stated that the

blood comes through the nose, but not from it. It is not unusual to find this condition in many of the acute infections, as measles, scarlet fever, diphtheria, whooping-cough, cerebrospinal meningitis, pneumonia, influenza, erysipelas, and small-pox, but it is especially noted in typhoid fever. In various cases of circulatory disturbance where the patient is beyond middle life, and there is an associated increase of blood-pressure, a passive congestion of the mucous membrane is invariably produced which predisposes to bleeding, especially from the vascular area in the anterior portion of the septum. Such cases are particularly noted in mitral and tricuspid stenosis, aortic insufficiency, disease of the coronary arteries, aneurism, cirrhosis of the liver, chronic interstitial nephritis, and arteriosclerosis, resulting in apoplexy or endarteritis obliterans.

When epistaxis recurs in elderly individuals it is in most instances a symptom of contracted kidney or of arteriosclerosis, and should not be passed over lightly. The writer cites cases in which this warning epistaxis, treated by tamponing without regard to the underlying trouble, has occurred a few weeks before apoplexy. Hummel (*Fortschritte der Med.*, Feb. 10, 1908).

Epistaxis in old age is due to one of the following conditions:—

*Arteriosclerosis*; it may be profuse and frequent, capable in either respect of causing death—happily most exceptionally—it occurs in sclerosis, preferably during cold weather, sudden changes of temperature, fits of coughing, and after severe or prolonged effort and hearty meals.

*Bright's disease* causes epistaxis in three ways, by the arteriosclerosis set up, the hypertension accompanying it, and the autointoxication giving rise to it.



*Different affections of the liver*—hepatic congestion, atrophic and hypertrophic cirrhosis, malignant or simple jaundice, cancer of the liver—bring about epistaxis by the sclerosis and by the dyscrasia often associated.

*Malarial disease*, chiefly in the cachectic stage, and *diabetes*, in all its phases, obtain their tendency to bleeding from the nose, partly from the sclerosis which they set up and in part from the alteration caused in the blood.

*Heart disease* has an influence upon the etiology of epistaxis. Aortic lesions act by means of the vascular changes and the hypertension; mitral and tricuspid affections produce it by the mechanism of stasis, which follows upon the earliest appearance of hyposystole.

*Cerebral congestion*, often the prelude to cerebral hemorrhage, shows itself, and can sometimes be estimated by the amount, more or less profuse, of the bleeding. A sudden stoppage of the hemorrhoidal function, for example, in arthritis, gives rise to attacks of "supplementary" epistaxis, such as by an analogous mechanism are also met with during the menopause.

*Hemophilia*, relatively uncommon in old people, comprehends epistaxis among the changes of its dyscrasia.

Lastly, apart from all causes general or, at all events, distant from the nasal fossa, place must be found for local causes, the chief of which in old age are *epithelioma*, *sarcoma*, *polypi*, *syphilitic ulcers*, and *varices* of the mucous membrane, sometimes amounting to the formation of capillary aneurisms. Ranzier (*Traité des maladies des vieillards*; Practitioner, June, 1910).

Diseases of the lungs, such as chronic bronchitis, emphysema, pleurisy with effusion, empyema, and tumors pressing on the lungs, may be predisposing factors. Hemophiliacs have long caused physicians much anxiety because of their tendency to

bleed, often on the least provocation, and of the difficulty frequently encountered to readily check the hemorrhage. Purpura, scurvy, and the secondary anemias sometimes add much to the danger of the patient, and the discomfort of the medical attendant, by the easy manner in which hemorrhage takes place. Vicarious menstruation has manifested itself by the escape of blood from the nose at the time of the menstrual period.

Notwithstanding the fact that a vigorous effort is usually made to check bleeding from the nasal cavities, one must not lose sight of the fact that such a condition may really be nature's safety-valve, as in cases of arteriosclerosis with increased blood-pressure; or that it may be the warning signal of the existence of cerebral hemorrhage, embolism, or thrombosis.

That cases are sometimes greatly benefited by the free flow of blood from the nose was evident in the report of 12 cases of cerebrospinal meningitis reported by Hays (*New York Medical Journal*, September 24, 1910, p. 605). In 4 of these cases epistaxis occurred, followed by a drop in temperature and the ultimate recovery of the patients. Of the remaining 8 cases, 3 succumbed to the disease.

The various changes which take place in the tissues in tuberculosis and syphilis not infrequently manifest themselves in the structures of the nose, and may sometimes result in nasal hemorrhage. Few of the drugs have been held responsible as being offenders, but distinct evidence has been produced against phosphorus, chloralamide, quinine, and the salicylic compounds.

Age, sex, and environment seem to be more or less significant in cases of

epistaxis. The common period for the more frequent occurrence of this condition is from about the second or third year to puberty. As a rule, the adult is singularly free, but the tendency for a recurrence may manifest itself again in old age. Altered atmospheric pressure, as in balloon ascensions, mountain climbing, and diving, or even the extremes of temperature, may have a decided influence.

In some cases no demonstrable cause can be determined, and these are classified as (3) *Idiopathic*.

Just why bleeding should take place under these various constitutional conditions may be due (1) to alterations in the constituents of the blood; (2) to some disease within the blood-vessel walls; (3) to some obstruction to the circulation causing a strain of the whole system, and the nose suffering first because the vessels are superficial and in places the veins are enlarged to cavernous sinuses; (4) to the fact that the blood may be a vicarious discharge, or may be caused by the lowered resistance of the tissues to various chemical and bacterial toxins, or to a pathological change within the mucosa as the result of a local infection, but caused by a general disease. There is a possibility that the toxins produced in diphtheria may act upon the terminal nerve-fibers within the blood-vessel walls, producing a paresis of the walls, localized engorgement, and consequent rupture of the nasal mucosa at the weakest spot. In some cases of infection, however, it seems evident that the hemorrhage is due to the diminished resistance of the patient on account of the toxemia.

**DIAGNOSIS.**—In the great majority of the cases the direct cause for

the nasal hemorrhage can be readily determined, but occasionally a case is encountered in which the evidence is quite obscure. The various infections and constitutional diseases will invariably give their associated symptoms. In the cases of hemorrhage as the result of high arterial tension, (1) the bleeding starts rather suddenly; (2) is usually profuse, often lasting for hours and frequently recurring at intervals of a few days until the blood-pressure is lowered; (3) the local treatment is seldom efficacious, and the usual styptics, cauterants, and packing prove to be of little or no avail unless measures of a general nature are instituted to reduce the tension. With the reduction of the excessive arterial pressure the hemorrhage ceases. In plethoric persons the bleeding may be preceded by headache; or in those persons prone to repeated attacks it may be produced by simply blowing the nose, sneezing, or introduction of the finger; or it may be spontaneous, even during sleep.

**TREATMENT.**—In the treatment of epistaxis there are several factors to be considered. As a rule, in the great majority of cases simple methods are readily efficacious; but if bleeding persists in spite of their application, search must be made for some constitutional cause. For instance, in cases of arteriosclerosis the blood-vessel walls are thickened and frequently contain deposits of lime salts, making it impossible for the necessary collapse to take place. At the same time the continuous stream passing over the ruptured spot usually does so with such force as to prevent any appreciable coagulation taking place.

Various remedies have been used in nasal bleeding, with more or less success in certain cases. A preparation of **cocaine**, gr. v (0.3 Gm.); **adrenalin**, mxx (1.25 c.c.); **aqua**, fʒss (15 c.c.)—sprayed into the nose—will invariably prove successful in the majority of the milder cases. However, one may resort to the insufflation of finely powdered **alum** or **tannic acid**, or the use of an 8 to 10 per cent. solution of the same drugs.

When it is difficult to locate the precise source of hemorrhage, an application of **adrenalin** to the anterior portion of the septum will blanch the whole mucosa except bleeding spots. These stand out clearly against the pale surface as red, circular areas. **Cauterization** of these spots with 90 per cent. **trichloroacetic acid** soon arrests the bleeding. W. Lapat (Jour. Amer. Med. Assoc., Oct. 14, 1916).

Solutions of **zinc sulphate**, **lead acetate**, or **copper sulphate**, gr. xxx to fʒj (2 to 30 Gm.), may be applied by syringe or pledgets; while **collodium** or a 10 per cent. **gelatin** solution may be smeared over the bleeding surface with a soft swab. Occasionally it is necessary to apply to the bleeding spot a solution of **silver nitrate**, gr. lx to fʒj (4 to 30 Gm.); a crystal of **chromic acid** fused into a bead on the end of an applicator, or even the **actual cautery**; but in resorting to any of these cauterants, one must guard against the marked destruction of tissue that may occur, and must aim as much as possible toward regeneration. When the bleeding is so profuse as to make it impossible to locate the area from which it is coming, douching of the nose with **hydrogen peroxide**, followed by a solution of **boric acid**, and then **packing** will frequently give gratifying results. In using the per-

oxide, however, the possibility of infecting the accessory sinuses must be remembered. Benefit is sometimes derived from using a hot douche of **phenol**, fʒj to Oj (4 to 500 c.c.) at a temperature of 105° to 130° F. (40.5° to 54.4° C.). A solution of **alum**, ʒij to Oj (8 Gm. to 30 c.c.), may be substituted with satisfactory results.

If necessary to apply pressure to the bleeding surface, it can readily be done with cotton or gauze, with or without one of the astringent solutions. Various preparations have been suggested for the impregnation of the gauze. A paste made by adding powdered **tannin** to a 20 per cent. solution of **antipyrin** has been used. **Beck's bismuth paste** has recently been advocated. Powdered **potassium permanganate** and **vaselin** appear to have adherents, while ʒj of **iodoform** to fʒj of compound tincture of **benzoin** has been used to advantage. If the gauze packing is soaked in sterile liquid **albolene**, and the patient given the same preparation and a dropper, and instructed to make frequent applications while in the recumbent position, it encourages healing and makes possible the easy removal of the gauze in twenty-four to thirty-six hours. The nasal chambers have also been packed with gauze soaked in **carbolyzed gelatin** solution. **Bernay-Simpson tampons** have been found extremely useful, especially if the bleeding is situated in the anterior portion of the septum. Casselberry suggests the insertion into the nose of a well-lubricated, clubbed-end, **rubber finger-cot**, and filling it with a yard or more of a 1¼-inch gauze.

A **tampon** is used by the writer, composed of compressed cotton modi-

fied from Simpson's tampon, three inches long by one-half inch wide by one-sixteenth thick, wrapped as in a cigarette with gutta-percha tissue, the free edge being gummed down by some sterile ointment except at the ends. These smooth-surfaced tampons are easily and usually painlessly removed; they are deemed safer and much better than trusting to local medicinal applications in cases of postoperative hemorrhage. Sterile water or salt solution should be dropped on the ends to cause the tampon to swell and fill the passage. Two can be used side by side in very wide fossa and they can readily be narrowed by clipping. M. D. Stevenson (Jour. Amer. Med. Assoc., June 4, 1910).

The inflated **Rose bag** may be used, but in severe cases it will not give sufficient pressure to check the hemorrhage. Boyd (Australasian Medical Gazette, January 20, 1910, p. 26) has used a 5- or 6- inch square of finely starched linen, and inserted it into the nose to the nasopharynx with a pair of forceps or a penholder, and filled it with cotton soaked in any styptic; even **vinegar** may be used to advantage. Porcher (New York Medical Journal, 1909, xc, p. 331) **clamps** both nostrils with a clothespin or a stiff, bent hairpin, in order to allow the clot to form.

The author has frequently had success with the following procedure, originally suggested by Naegli: The patient sits upright in a chair, and the operator, standing behind him, places the index fingers of both hands beneath the body of the lower jaw on each side, while the thumbs rest behind the angles. Gentle traction is then made upward upon the head, which is simultaneously extended backward as far as the patient can comfortably bear, thus putting the muscles of the neck on the stretch. An **artificial anemia** is thus set up in

the vessels of the head and also in the smaller vessels of the nasal mucous membrane, causing the epistaxis to cease. The procedure should not be continued longer than from one to two minutes, or a partial or complete loss of consciousness may result. Ritschl (Munch. med. Woch., Oct. 22, 1912).

On rare occasions it is necessary to insert a **gauze plug** into the nasopharynx. This is best done by passing a rubber catheter through the bleeding nostril to the postnasal space, pulling it forward in the mouth with a pair of forceps, fastening a piece of tape of at least a foot or more in length, with a gauze plug tied in the middle, and pulling the catheter back through the nose, at the same time guiding the plug with the index finger as it enters the nasopharynx. The nasal tape is pulled taut and tied firmly to a plug at the anterior nares. The end of the tape emerging from the mouth, to be used in removing the plug, is fastened loosely to the ear.

Apoplexy may result from plugging in epistaxis. A number of cases reported in which this has been the result, especially in the aged. In one case plugging with perchloride of iron produced erysipelas with very grave symptoms. Nasal hemorrhage opening the vessels of the nasal mucous membrane lowers the threatened arterial hypertension, frequently relieving the vessels of the brain and conducing to the safety of the patient.

The treatment should not be begun by plugging the anterior and posterior orifices. In young persons with healthy arteries this might be permissible, but plugging the nasal fossa in aged persons is dangerous. Perchloride of iron should never be used. Simple methods should be tried first, as **pinching the nose, elevation of the arms, cold water, key down the back, etc.** Afterward small **plugs steeped**

in a solution of antipyrin may be applied through the anterior nares, or the nasal passages may be irrigated with hot water. These methods will moderate the hemorrhage. Dry cupping in the lumbar region, purgatives, mustard footbaths, applications of hot water to the abdomen should all be resorted to before plugging. Landouzy (Medical Press, July 1, 1903).

The writer injected hypodermically  $\frac{1}{2}$  grain (0.03 Gm.) **emetine hydrochloride**, and in 20 minutes the hemorrhage ceased entirely. Prestley (N. Y. Med. Jour., May 2, 1914).

If **tampons** are at all resorted to, their long retention within the nose should be avoided, to eliminate the possibility of infection of the accessory sinuses; and, when inserted, should always be preceded by insufflation of powdered **bismuth subnitrate**, to avoid decomposition of the secretions.

The use of **Bellocoq's cannula** should be reserved as last resort, as the instrument is very likely to cause injury, with secondary inflammation. The ears must be very carefully watched, and with the first signs of reddening of the drum membrane the packing must be removed. Thus the writer has seen several cases of otitis media with mastoiditis, and also empyema of the antrum, after the use of Bellocoq's cannula. O. Mayer (Münch. med. Woch., Nu. 43, 1909).

It is frequently questionable as to whether the internal administration of medicines is of any benefit. Hypodermic injections of **morphine** have been advocated, and seem to work to advantage in keeping the patient quiet, even if not exerting a hemostatic action. In case of bleeders, when the arterial pressure is low, large doses of **strychnine nitrate** sometimes appear highly beneficial. Resort may also be had to the internal administration of powdered **opium**,

gr. j (0.06 Gm.), with **lead acetate**, gr. ss (0.03 Gm.), repeated hourly for three doses, which shows a tendency to coagulate the blood. If the blood-pressure is normal, the administration of **adrenalin chloride**, gtt. v (0.3 c.c.) in water—every fifteen minutes—may work to advantage. Ten drops of a 1:2000 solution have been injected into the upper lip, on the side corresponding with the bleeding, and brilliant results have been reported. The internal administration of **gelatin** and the **calcium salts** is of doubtful benefit. Instances have been reported in which **serum** has proven beneficial, even **diphtheria antitoxin** being resorted to in an emergency. **Atropine** hypodermically is also effective.

In recurrent epistaxis the cause should be sought. The diet should be supervised, constipation corrected and all forcible movements avoided. The best drug to use is **digitalis**, usually in form of the titrated infusion. As a rule 0.7 to 0.8 Gm. (11 to 12½ grains) of digitalis given during two or three days is all that is necessary. Among 84 cases treated in this way, a recurrence of the hemorrhage was seen in only 2, where there was a tendency to hemophilia. The author believes that this excellent effect of digitalis is not due to any specific action, but that the drug merely overcomes the venous stasis and distributes the blood better over the body. Focke (Therap. d. Gegenwart, Sept., 1910).

Besides the well-known position with **ice** upon the nape of the neck, he advises internally 40 Gm. (1½ ounces) of 10 per cent. **gelatin** (calf's foot), which also can be given intramuscularly; furthermore, internally, 1 tablespoonful in milk, to be given every half-hour of the following: **Calcium chloride**, 4 Gm. (1 dram); syrup of mint, 50 Gm. (1½ ounces); water, up to 250 Gm. (8 ounces). A

hypodermic injection of a rather strong dose of **morphine** has often good effects. Instead of morphine, **sodium chloride** up to 20 or 30 Gm. ( $\frac{3}{4}$  to 1 ounce) may also be given, and **sodium bromide** up to 15 or 20 Gm. ( $\frac{1}{2}$  to  $\frac{3}{4}$  ounce). Kobrak (Med. Klinik, June 2, 1912).

**Submucous resection** advocated in habitual nosebleed and with a perforating ulcer of the septum. Gallusser (Schweizer med. Woch., Mar. 20, 1926).

The patient should receive supportive treatment and careful nursing until health and strength are restored.

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**ERGOT.**—Ergot is a blight, the sclerotium of a parasitic fungus (*Claviceps purpurea*) which attacks and finally supplants the grain in the common rye (the *Secale cereale*). It is popularly known as "spurred rye," or "cockspur." It presents itself in grains of a slightly curved, fusiform shape, which are brittle, yet moderately flexible. Externally, it has a purplish-black color with longitudinal furrows on each side. It should be moderately dried, and should not be exposed to a damp atmosphere. It has a disagreeable, fishy odor, and a somewhat bitter, acrid taste.

Ergot is a complex substance containing a number of active principles, the most important of which are: *ergotoxine*, an alkaloid which is both a vasoconstrictor and stimulant of the uterus; *parahydroxyphenylthylamine*, or *tyramine*, a feebly basic epinephrine-like, strongly vasoconstrictor substance; *betaminazolythylamine*, or *histamine* (*ergamine*), even in great dilution, a powerful contractor of the uterus; *isoamylamine*, also a vasocon-

strictor, but occurring in too small a proportion in ergot to influence materially its action.

Ergotoxine is a highly active alkaloid, having the properties of ergot most desired in medicine. It brings about a long-enduring contraction of the walls of the arterioles, and increases the movements of the uterus. Its action is feeble when given by the mouth, but it is more marked in subcutaneous injections, and much more so when given intravenously. The last-named method is recommended in cases where a rapid and certain action is desired, either in **shock** or in **post-partum hemorrhage**. W. H. Cronyn and V. E. Henderson (Jour. of Pharmacol. and Exper. Therap., Aug., 1909).

Ergotoxine acts more rapidly than the fluidextract and it can be given hypodermically. Ergotinine, however, is inert and useless. J. Gordon Sharp (Proceed. Royal Soc. of Med., May, 1911).

Recent work by various investigators, particularly Barger and Dale, has recently elucidated the composition of ergot and shown that ecboline, sphacelmic acid, cornutine, sphacelotoxin, and other familiar active principles so-called were mixtures of the above and other principles in an impure form.

Number of tests of fluidextracts of ergot obtained from representative manufacturers, with the result that only two out of eleven samples were found to be active. The writers point out the mistake of the general idea that fluidextract of ergot is a stable preparation; in point of fact it deteriorates very rapidly. Wood and Hofer (Univ. of Penna. Med. Bull., Feb., 1909).

Most galenical preparations of ergot contain considerable amounts of the active principles, but do not show any great or marked action when given by the mouth. The doses usually recommended for these prepara-

tions are much too small. When injected intravenously a fall in blood-pressure always precedes the rise, except after the administration of ergotoxine. Cronyn and Henderson (Jour. of Pharmacol. and Exper. Therap., Aug., 1909).

Ergot and its alkaloids deteriorate rapidly on keeping, the fluidextract of ergot, for instance, losing on an average about 10 per cent. per month. This may be avoided, however, by keeping it in vacuum ampoules.

The ergot on the market varies greatly in its active principle, i.e., in its power to cause unstripped muscle stimulation. A perfectly prepared fluidextract rapidly and continuously loses its activity and becomes worthless. The crude drug also loses its activity on keeping. Therefore, all liquid preparations of ergot should be kept in small bottles, hermetically sealed, and even then the label should declare at what date it is manufactured, since, if a preparation is old, it is of but little value. Ordinary fluidextracts, even if not exposed to the air, will lose approximately 10 per cent. of their strength per month. Wood and Hofer (Arch. of Intern. Med., Oct., 1910).

The ergot alkaloid was found by the writer to paralyze selectively all the sympathetic nerve endings. The same antagonism that exists between the action of pilocarpine and atropine for the parasympathetic nerve endings exists between adrenalin and the ergot alkaloid. E. Rothlin (Klin. med. Woch., July 23, 1925).

### PREPARATIONS AND DOSE.

—*Ergota*, U. S. P. (ergot). Dose, 30 grains (2 Gm.).

*Fluidextractum ergotæ*, U. S. P. (fluidextract of ergot). Dose, 30 minims (2 c.c.).

*Extractum ergotæ*, U. S. P. IX (extract of ergot), which is incompatible with astringents and metallic salts in solution. Dose, 4 grains (0.25 Gm.).

*Vinum ergotæ*, U. S. P. VIII (wine of ergot). Dose, 2 fluidrams (8 c.c.).

*Extractum ergotæ aquosum*, N. F. (ergotin; aqueous extract of ergot). Ergot is extracted with chloroform water, and the extract treated with alcohol and evaporated to a pilular consistence. Dose, 3 grains (0.2 Gm.).

Various other purified preparations of ergot, such as *cornutol*, *ergone*, *aseptic ergot*, as well as the three chief active principles themselves (see above) are on the market. *Ergutine* is a mixture of these three principles.

**Subcutaneously.**—Bonjean's *ergotine* (Fr. Cod.) and Squibb's *ergotine* are especially prepared for hypodermic use, 5 parts being dissolved in 7 parts each of glycerin and water and then filtered, 3 to 12 grains (0.2 to 0.8 Gm.—representing 120 grains—8 Gm.—of crude ergot) of the *ergotine* being the proper dose.

Ammonia is said to be the best solvent for the active principles of ergot, 2 parts of the former to 1 of the latter being used, and the dose being 60 minims (4 c.c.).

### PHYSIOLOGICAL ACTION.—

Applied locally to mucous membranes ergot acts as a somewhat irritating astringent and hemostatic. On the skin these effects are very slight if at all appreciable.

Taken internally by the mouth ergot is absorbed with fair promptness, its action becoming manifest in from fifteen to twenty minutes and lasting about one hour. *Intravenously*, a moderate dose produces a marked rise of the blood-pressure; but if the dose be large, the rise is preceded by a fall of short duration. Very large doses or too frequently repeated doses may thus lower the blood-pressure below normal.

The changes in the blood-pressure are mainly cardiac. This is confirmed by myocardiograms from the intact and excised heart. Ergot causes first a lessening and then an increase of the excursions; both phenomena may occur while the ergot is being injected. The rate of the heart is but little altered. The effect of ergot must be exerted directly on the cardiac muscle. There is some oncometric evidence that ergot has a slight vasoconstrictor action, but this is inconstant and inconsiderable. There was no evidence of strong constriction or of a high rise of blood-pressure.

The preliminary fall of blood-pressure is absent if the ergot is given by intramuscular injection.

The action of ergot is independent of the dose, within wide limits. The relative predominance of the fall and rise differs somewhat in different ergot preparations; age, however, does not impair the efficiency of their action on the mammalian circulation. The effects are greatly diminished by lowering the blood-pressure, by any method. Shortly after the destruction of the spinal cord, however, ergot produces a relatively good rise of pressure.

Large doses of ergot depress the vagus center and the vasomotor endings. It is not acutely fatal, even in very large doses. Torald Sollman and E. D. Brown (*Jour. Amer. Med. Assoc.*, July 22, 1905).

In many species ergotoxin exerts a specific influence on the heat-regulating center, disturbing the relation between heat production and heat dissipation. In cats and in rabbits this induces a rise of body temperature; in rats, mice and pigeons it causes a fall. Githens (*Jour. of Pharm. and Exper. Therap.*, Nov., 1917).

**Circulation.**—The general effect of therapeutic dose is to constrict the peripheral blood-vessels, mainly through a direct action upon them and slightly by stimulating the vasomotor center, and thus to cause a

general rise of the blood-pressure. The heart is also stimulated by moderate doses, but depressed by large ones. Its rate is usually slowed through stimulation of the cardio-inhibitory center and the amplitude of the beats increased. These effects do not always occur, however, if the crude drug is used, since the histamine and certain other substances contained in it—choline, for instance—which tend to dilate the blood-vessels, may counteract the vasoconstrictor effect of the main active principles.

Ergot possesses the power to produce gangrene of the extremities. This is well shown by its action on the comb and wattles of roosters. This was formerly attributed to spasm of the arterioles, but is now believed to be due to the formation of emboli which obstruct the circulation.

**Uterus.**—Ergot powerfully stimulates the uterus and produces contractions through a local action on the motor endings of the hypogastric nerves, and also partly through excitation of the spinal "parturient" center. While small doses accelerate and strengthen uterine contractions large doses prolong the latter, finally converting them into tetanic spasms of long duration. As the various active principles in ergot possess a so different action on the uterine vessels according as to whether the uterus is pregnant or not—parahydroxyphenylethylamine, for instance—causing contraction of the pregnant uterus and relaxation of the non-pregnant organ, the effect of a given preparation is apt to vary according to the relative quantity of each principle it happens to contain; but inasmuch as the pregnant uterus is caused to contract more or



less by all the active principles, and the use of ergot in connection with this organ is mainly in parturition, this action alone need interest us.

Ergot acts in **labor** in the following manner: (a) It collects the small irregular and non-effective pains into larger effective contractions, so that the labor is sooner ended and the uterus saved work. (b) It improves the tone of the muscle-fibers, whereby the uterus gains an advantage in that its musculature is ready at once to respond to further contraction, and thus neither time nor energy is spent in bringing the fibers up to that point at which contraction begins. (c) By acting on the abdominal muscles and on the muscular system generally, the tissues as a whole are improved in tone. This helps the uterus in its struggles.

The foregoing may be called the immediate benefits, but there is often a more remote beneficial action. (d) The forcible contractions following the administration of ergot, by expelling uterine contents, such as after birth, membrane, or other foreign body, relieve the organ of its troubles and set it free to recover itself in the ordinary way of nature. J. Gordon Sharp (Proceed. Royal Soc. of Med. of London, May, 1911).

**Muscular System.**—Through a specific action upon all the involuntary muscular fibers, ergot tends to stimulate the myocardium, the gastric and intestinal muscular coat, the bladder, the pupil, and all other structures provided with this class of fibers. Ergot thus tends to favor cardiac contraction, gastric and intestinal peristalsis, micturition when due to cystic atony, etc., besides acting on the blood-vessels as stated under the appropriate head.

Ergot is a stimulant to all the unstriped muscle tissue of the body. As a part of this general action there is a stimulant effect on the arterial

muscles and probably also on the heart. The action on the blood-vessels occurs after destruction of the vasomotor center and, therefore, must be the result of an effect on some portion of the peripheral vasomotor mechanism. Wood and Hofer (Arch. of Intern. Med., Oct. 15, 1910).

**Elimination.**—The fate of the active principles in the body is unknown.

Ergot was found in the feces of several different persons and dogs by the writer after its administration by the mouth. The microscopic findings were positive even after a single dose of 1 Gm. (15 grams). The findings were positive only during from twenty-four to thirty-six hours after the ergot had been ingested. Strasburger (Centralbl. f. Gynak., Bd. xxx, No. 49, 1907).

**POISONING BY ERGOT.**—**Acute ergot poisoning** is very infrequent. Very large doses of ergot produce symptoms of gastrointestinal and cerebrospinal origin. When taken by mouth ergot produces a heat and dryness of the throat, thirst; gastric pain, with nausea or vomiting; intestinal colic and diarrhea, giddiness, headache, restlessness and even delirium, coldness of the surface of the body, dilatation of the pupils, with slowness and slight weakness of the pulse.

Tetany following poisoning by ergot, taken to cause abortion, was observed by the writer. Within 10 minutes of the administration of 15 grains (1 Gm.) of **chloral hydrate** and 30 grains (2 Gm.) of the **triple bromides** per rectum, full consciousness returned, and the spasm of hands and feet began to relax. Emsheimer (N. Y. Med. Jour., Dec. 18, 1915).

Children and pregnant women are the first affected when rye bread containing ergot is eaten, sometimes only after several days.

Death may occur from cardiac paralysis.

The writer witnessed the following typical case of ergot poisoning: Early one morning he was summoned to a woman who was in a comatose condition. The pulse was 58, small, weak; respiration was labored; temperature 98° F. (36.7° C.). It was noted that the flexor muscles of the forearm underwent severe tonic contractions at intervals of a few minutes. Later the flexor muscles of the thigh and legs showed the same appearance. The toxic condition came on a short time before the patient was seen, and was initiated by giddiness and convulsions. The fluidextract of ergot had been taken in dram (4 Gm.) doses every four hours for four days before the symptoms developed. The patient was removed to the hospital, where she remained unconscious for three days. Constipation was marked, but urination was free. The pupils were widely dilated. Purpuric spots appeared on the neck, arms, and limbs. The pulse at one time was as low as 56, and for two weeks never went above 70. The patient ultimately recovered. F. M. O. Gorman (Phila. Med. Jour., Oct. 13, 1900).

Case of a man who had difficulty in breathing in the morning. The pupils were dilated, and the power of accommodation almost completely lost. It was then found that he had been taking extract of ergot. The patient was, therefore, given a vigorous diet, the ergot stopped, and he soon recovered. Schneider (Münch. med. Woch., Sept. 30, 1902).

**Chronic ergot poisoning or ergotism**, was formerly rather common, occurring in epidemics as a result of eating rye bread containing ergot. As the poorer classes of Spain and Russia relied mainly upon rye bread for their food, it was among them that ergotism was most frequently met. Two types of chronic ergot poisoning are encountered, the gangrenous and the convulsive.

*Gangrenous ergotism* usually affects the peripheral structures such as the fingers, toes, nose, ears, and sometimes an entire hand or foot, leg or arm, the genitalia, and also various internal organs. Cutaneous phenomena—tingling, formication, redness, coldness, an earthy hue, an eruption of vesicles containing a dark, ichorous fluid, and dry gangrene—follow one another in more or less rapid succession, muscular contractions complicating in a large proportion of cases. Nausea, vomiting, diarrhea, and colic are also observed.

*Convulsive ergotism* manifests itself mainly by disturbances of sensation, headache, a hard and small pulse, painful muscular cramps, and even by epileptiform convulsions, which are followed by marked nervous depression. These salient symptoms may be preceded by vertigo, tinnitus aurium, headache, itching, burning, and crawling sensations in the skin. Mental phenomena are common, the patient becoming somnolent, stupid, irresponsive and apathetic. Mania, melancholia, and other forms of insanity may be simulated.

In 17 cases of psychoses from ergot poisoning witnessed by the writer, there did not seem to be any characteristic somatic feature of the ergot psychoses. The knee-jerk was variable, as also the sensory phenomena; exaggerated muscular excitability was more constant. The milder psychoses were not accompanied by any physical symptoms and in the severer cases the syndrome resembled actual tabes. The main cerebral features of the ergot psychoses were disturbances in consciousness and the emotional sphere, with more or less intellectual weakness and apathy. M. J. Gurewitsch (St. Petersburg med. Woch., Bd. xxxvi, S. 434, 1911).

Muscular tremors and contractures, especially of the flexors of the fingers and toes and of the extensors of the arms and thighs, are common. The majority of the symptoms of tabes may be present along with marked lassitude and emaciation. The organs of special sense are blunted, and the pupils dilated, though sometimes unequally.

**Treatment of Ergot Poisoning.**—

In *acute poisoning* the bowels should be opened by quick purgatives: by **castor oil** or **Epsom salts**. **Tannic** or **gallic acid** should be given internally. The **recumbent posture** should be maintained, the patient be stimulated with **brandy** or other spirits, and given **amyl nitrite** by inhalation.

In *chronic ergotism* the treatment is chiefly hygienic and symptomatic on lines similar to those that apply to the acute form. In the gangrenous form the treatment is operative, it being advisable to wait for a line of demarcation and then to **amputate** immediately above the line. **Saline solution** intravenously should be tried, however, before operative procedures are resorted to if as soon as the cutaneous phenomena suggesting the possibility of oncoming gangrene appear. **Hypodermoclysis** is indicated in all cases as soon as the diagnosis of ergot intoxication is made.

**THERAPEUTICS.**—Ergot is mainly used by obstetricians and gynecologists to cause uterine contraction. Its use as an oxytocic is sanctioned by very few authorities.

**Labor.**—Full doses of ergot are never to be given to hasten the delivery of a fetus, because it causes tonic contraction of the uterus, interruption of the placental circulation, endangering the child through as-

phyxia, and if operative procedures be necessary they are greatly embarrassed by the rigidity of the uterus, and the danger of the uterine rupture is increased. There is a possible exception to this restriction. It may be given as a prophylactic against postpartum hemorrhage during the second stage of labor in those cases in which it is indicated, but not if there is any mechanical obstacle to delivery, or if the fetal head is high up in the canal. If it is given during this stage of labor the fetal heart should be carefully watched, and instrumental delivery resorted to if any signs of asphyxia occur. If ergot is given before the membranes have ruptured, it may prevent further dilatation of the uterus and deprive the fetus of its blood-supply. The drug may produce its effect prematurely if given at the time of passage of the child's head, and thus interfere with the expulsion of the placenta by producing hour-glass contraction.

Instance of severe complications on account of the administration of ergot before the placenta had been expelled. The writer found 7 similar cases in German literature. In his own case delivery had been normal; two hours later the cervix permitted passage of two fingers and there had been considerable hemorrhage, but no signs of severe anemia, no dizziness nor fainting. As there seemed to be no change in these conditions, in a few hours the attending physician gave ergot and sent the patient to the hospital, where the cervix was found nearly closed. By this time fifty-five hours had elapsed since delivery of the child and there was a slight rise in temperature. After introduction of the inflatable bag for a few hours the placenta was evacuated by hand. Recovery promptly ensued. Schmid (Münch. med. Woch., Sept. 19, 1911).

The uses of ergot in parturition may be summarized as follows: (1) during labor, immediately after the birth, to keep the uterus firmly contracted and prevent post-partum hemorrhage; (2) earlier in labor, in occasional cases, to overcome dangerous inertia; (3) in subinvolution of the uterus.

It is especially indicated if an anesthetic has been required to effect delivery. It is useful as a prophylactic against, and a remedy for, post-partum hemorrhage.

The fluidextract administered by the mouth is generally preferred. When rapid effects are necessary, ergot may be given intramuscularly in preference to the subcutaneous method, which gives rise to considerable pain. A good preparation of ergotin in 10-minim (0.6 c.c.) doses may be employed for the purpose. Several new preparations, *ernutin*, *ergone*, and *aseptic ergot*, are particularly adapted to hypodermic use.

To obtain the greatest therapeutic value of ergot in labor, it should be limited to, or near, the end of the third stage, administered by the mouth when indicated for the prevention of hemorrhage, and hypodermically when indicated for the control of hemorrhage. Applegate (Amer. Med., June 24, 1905).

**Abortion.**—Ergot is useful in this condition when the uterus remains relaxed, but is contraindicated before the uterus has been emptied. It is also useful in the subinvolution consequent upon abortions, given continuously in small doses.

**Nervous Disorders.**—Ergot has also been found useful in certain mental diseases, as **epileptic mania** when associated with cerebral hyperemia, and **chronic mania** with lucid intervals. When given in large doses in **acute**

**myelitis**, and in **congestion of the spinal cord and meninges**, it is said to be of value. Merits have been claimed for it in the treatment of **delirium tremens**, in conjunction with the bromides.

There is but one real indication for the multiple uses of ergot, which is the contraction of weak and relaxed unstriated fiber or other vital contractile tissue. By applying it ergot will be found a useful remedy in a large variety of cases, medical as well as surgical. Among these are affections of the heart, blood-vessels, and atony of the hollow viscera. It may be used to promote elimination and assimilation, to increase impaired functional activity, to regulate the menstrual functions, to counteract **insomnia**, **shock**, **neurasthenia**, **spasmodic nervous conditions**, **paralysis**, **coma**, **pain**, **toxemias**, **acne rosacea**, **varicose veins**, nervousness with defective venous circulation associated with **excessive cigarette smoking**, and surgical conditions. Alfred Livingston (Med. Rec., Nov. 23, 1907).

In **hypertrophy of the prostate**, particularly the form due to senile influence, the vasoconstrictor action of ergot may be used with benefit.

In 2 cases of **enlargement of the prostate**, 1 a senile enlargement and the other a traumatic inflammation in a young adult, the administration of ergot apparently reduced the obstruction caused by the enlarged organs. The writer urges the more frequent use of ergot in these cases. He gives 1 dram (4 Gm.) every 4 hours. Murphy (Pract., Nov., 1918).

**Hemorrhage.**—In internal hemorrhage of various internal organs, especially in hemoptysis, ergot has been used because it contracts the blood-vessels in the bleeding area and tends to favor clotting. Inasmuch, however, as vasoconstriction occurs in all parts of the body, a general rise of the

blood-pressure is produced which tends to counteract what hemostatic action it might have through its effect on the bleeding vessels. Its use therefore is no longer advocated in hemoptysis nor in cerebral hemorrhage, i.e., apoplexy. In renal and subcutaneous hemorrhages, however, ergot has proven its value experimentally and clinically. Hence the fact that it is effective in pulmonary edema (but usually given with atropine) in epistaxis, hematuria (renal or vesical), purpura hemorrhagica, the hemorrhage of scurvy, etc. It has been used also in the intestinal hemorrhage of typhoid fever, in dysentery with bloody stools, in serous diarrhea, and in bleeding hemorrhoids.

Ergot may possibly effect a cure in small aneurisms of peripheral main arterial trunks by the contractions produced as the result of its action on the unstripped muscular fibers in the affected portion of the vessel. It also promotes coagulation of the blood in an aneurismal sac.

**Diabetes.**—Hypodermic injections are sometimes of value in diabetes mellitus to reduce the excessive flow of urine by causing vasoconstriction. The use of ergot combined with the bromide of sodium has been advised by Hare in the treatment of diabetes insipidus.

**Genital Disorders.**—Ergot has been employed with good effect in spermatorrhea and in deficient tone of the genital organs.

Locally ergotin is of value in conjunctivitis, incipient boils, and may be used in suppositories in such conditions as prolapsed rectum and hemorrhoids.

Clemins has used injections of ergot (4 grains to the ounce) into the blad-

der in the cystitis of paraplegic patients. The fluidextract may be employed as a local application in chronic follicular tonsillitis, and the oil is said to be of value in the treatment of seborrhea.

Ergot is used in enlarged prostate with retention of urine and in enuresis. Hypodermic injections about the dorsal vein of the penis are useful in impotence when relaxation of the organ occurs too early as a result of the too prompt return of the excess of venous blood to the general circulation.

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AND

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## ERIGERON, OR FLEABANE.

—Oil of erigeron is a volatile oil obtained from the fresh, flowering herb of *Erigeron canadensis* Linné. It is of a pale-yellow color, having a peculiar, persistent, aromatic odor, and a slightly pungent, aromatic taste. As the result of age or exposure to the air it becomes darker and thicker. The specific gravity ranges from 0.845 to 0.865.

### PREPARATIONS AND DOSE.

—*Oleum erigerontis*, U. S. P. VIII (oil of erigeron) is given in the dose of 15 minims (1 c.c.). It is best given in capsules. It is soluble in an equal volume of alcohol.

**PHYSIOLOGICAL ACTION.**—Oil of erigeron is an astringent and an active diuretic, being similar in action to turpentine, but less irritating. It is non-irritating to the stomach, and is said to have a slight tonic action.

**THERAPEUTICS.**—Externally, oil of erigeron may be applied to prevent insects from stinging, biting, or otherwise injuring the skin. Owing to its astringent action, oil of erigeron may be given internally for hemorrhages of a moderate degree. It is of most value in the treatment of passive uterine hemorrhages or oozing, and is also useful in epistaxis. In combination with cubebs and copaiba, it has also been used in the later stages of gonorrhea. In the treatment of dysuria, especially when occurring in children, the use of this drug will be found

of value. It may also be used in **diarrhea**, **dropsical affections**, and in chronic forms of renal disease, its use being contraindicated in acute congestions of the kidney. H.

### **ERYSIPELAS. —DEFINITION.**

—By erysipelas is meant a violent inflammation of the superficial lymph-channels.

**SYMPTOMS.**—Erysipelas is most frequently found about the face and head, probably because of the excessive number of superficial lymphatic vessels. The affection has gradually lessened through the use of antiseptic principles in surgical practice.

It may occur in or extend to the fauces and tongue and, extending painlessly up the Eustachian tube, involve one or both eyes and may cause blindness (Snell). It has been observed, in fact, in all parts of the body.

The many different skin lesions which may be found so often upon the legs of old men, such as eczema, etc., may be the starting point for the erysipelas infection. The skin of old men become easily penetrable by the streptococcus, and the itching to which the skin lesions give rise, as well as the frequent slovenliness of old men, are contributing causes which also explain the frequency of the infection. Lucien and Parisot (*Semaine méd.*, Dec. 11, 1907).

The writer has encountered 6 cases, all in men who had recently slaughtered a hog with swine plague. The incubation period ranged from 24 to 30 hours. Pain was the first symptom to attract attention, but the **exanthem** and **lymphangitis** are the most characteristic features. Svith (*Ugeskrift f. Laeger*, Jan. 24, 1918).

True cutaneous erysipelas is characterized by severe elevation of temperature, attended by a disseminated inflammation of the skin. This is sometimes preceded by a chill. The

elevation of temperature continues until the erysipelatous process reaches its end. There may be a wound from which the redness starts, or there may be no cutaneous evidence of the seat of infection. A mere scratch, though healed, may have allowed the streptococcus to enter; having travelled up the lymphatics, the organism starts the erysipelatous process at a distance from the seat of entrance.

Case in which a judgment for \$5000 accident insurance was granted on the plea of accident, the death of the insured having been caused by erysipelas due to a slight injury on his cheek, causing a slight abrasion of the skin, which resulted in traumatic erysipelas. The attending physician testified to the discovery of the abrasion of the skin, and that in his opinion the disease from which the assured had died was wholly infectious, and could not have resulted except through infection of some wound or abrasion of the skin; that it made its first appearance at the edges of the alleged wound, and that in his opinion it resulted solely from the infection of that wound. (*Jour. Amer. Med. Assoc.*, Sept. 21, 1912).

There may be red streaks showing lymphatic glands extending from the wound to the special place where the poison now develops very freely.

In the newborn, according to Lemaire, erysipelas may develop not only about the umbilical wound, but also around a vaccination wound and around the conjunctiva. Histological examination shows accumulations of streptococci in the lymphatic vessels. There may be a few bacilli in the superficial region of the derma, but none in the epidermis. At first the fever is not excessive, and it may not be noteworthy until the second or third day. If the child does not quickly die there may be several resulting

abscesses, and death may ensue from the fifteenth to the twentieth day. If recovery follows it may be long in coming, being delayed by athrepsia or infectious diarrhea.

Erysipelas in the newborn infant is a very serious and generally fatal disease. Its fatality depends on the absence of reaction against the germs, due to the absence of phagocytosis in the newborn child. After the age of 3 months the prognosis is quite otherwise because here phagocytosis goes on normally. Starting from the solution of continuity at the umbilicus the germs enter the tissues and are not opposed by the lymphatic glands. They enter the lymphatics of the subcutaneous tissues, where they are found in great numbers, as also in the outer coats of the blood-vessels. A rapidly fatal peritonitis closes the scene. The external redness and swelling are slight. A. Herrgott (*Annales de gynéc. et d'obstet.*, May, 1908).

The writers observed 7 recoveries among 12 infants with erysipelas, all only a few days old, after using Delbet's *bouillon-vaccine* treatment. Only 1 recovered of 12 treated by the ordinary measures. Boidin and Tierny (*Bull. de la Soc. Méd. des Hôp.*, Feb. 11, 1921).

Tension of the cellular tissues now becomes very marked; blebs may form on the surface from the intense irritation of the papillary layer of the skin. It sometimes happens that the process, having started in one part of the body, may be arrested, only to manifest itself elsewhere. As a rule, after the process subsides the parts are soon restored to their normal condition, although a certain amount of desquamation takes place.

When the deeper lymphatics are affected a great deal of effusion takes place in the cellular tissue, and cellulitis results, which is much more in-

tense than that described as arising from the streptococcus in its ordinary degree of virulence. It bears, however, a great analogy to it, only the symptoms may be much more intense. A suppurative process takes place with a great disintegration of cellular tissue. This has been characterized as phlegmonous, or suppurative, erysipelas. It may come to the surface, and subsequently change its course as an erysipelas of the skin. It is also possible that other bacteria should contaminate this infection.

The constitutional symptoms correspond to the intensity and extent of the local process. The temperature rises to about 104° F., and may reach 107° F. The fever may be of a continuous remittent or intermittent type, and is in direct proportion to the extent of the inflammation. In some instances there occurs no fever, a probable sign that the immunizing functions are inadequate.

Two cases in which the temperature was for the most part subnormal, although in both the cerebral symptoms were early and profound, one being an elderly man and the other an infant 3 weeks old. Macauley (*Brit. Med. Jour.*, Feb. 26, 1910).

Gastric symptoms may likewise occur, with loss of appetite, nausea, vomiting, excessive thirst, and a highly coated tongue. The urine is generally dark colored, and may contain albumin, blood, bile-pigment, and micrococci. The spleen is sometimes swelled, and there may be pain in the region of the kidneys. An infective pneumonia due to extension of the disease from the oral cavity or pharynx may likewise occur. The heart is also involved in a large proportion of cases.

Of 2664 cases of erysipelas in the writer's service at Vienna, 288, that is, 10.8 per cent., were in persons over 60. Only 91 of his elderly patients were men. He has been making a special study of the affection in the aged. Complications on the part of the respiratory organs were no more common than after other infections, but kidney affections were repeatedly encountered with erysipelas in the elderly, especially an acute hemorrhagic process subsiding with the infection. Nervous symptoms were frequent. The erysipelas attacked the face almost invariably; none of the patients presented erysipelas of a mucous membrane, although he knows of 1 case on record in which the throat was primarily invaded. Unusually frequent were the complications or sequels in the form of suppurative processes in the subcutaneous cellular tissue, especially when the erysipelas was on the limbs. Gangrene of the lids was observed in a few cases, but the eyeball did not suppurate in any instance, and he witnessed the healing in some cases of a deep, extensive gangrenous process, even in women over 80. In 25 per cent. of his 288 cases of erysipelas in the elderly, it terminated fatally. H. Schlesinger (*Med. Klinik*, Aug. 8, 1909).

Erysipelas influences the myocardium. In about 500 patients with erysipelas examined, the writer found myocardial changes in about 250, and dilatation of the heart in 44 patients. The changes pass away with the erysipelas without apparently leaving permanent injuries. The only physical sign seems to be the change in the outline of the heart. Teissier (*Semaine méd.*, Jan. 12, 1910).

Case of a healthy girl of 16, tending a woman with a severe erysipelas of the face, who was suddenly taken with serious peritonitis and succumbed on the fifth day. The autopsy revealed an acute streptococcic seropurulent peritonitis, but no sign of perforation; the genital organs were normal. M. Vallas (*Lyon méd.*, Oct. 9, 1910).

Out of 6 cases of erysipeloid, Rahm cultivated the swine bacillus in 2, Duttman in 7 out of 9, and Diemer out of 3 found it in every case. The writer examined 5 undoubted instances of erysipeloid. Four of these workers were "smoke dryers" and "butcher's" assistants, and the fifth was largely engaged in handling pork. Of the 5 examined the swine erysipelas bacillus was successfully isolated, tested and cultivated in 3. D. Acel (*Deut. med. Woch.*, July 16, 1924).

Case in which a child, aged 10, died from chronic septicemia which responded to tests for swine erysipelas. This disease occurs in other domestic animals and in poultry. Postma (*Ned. Tijds. v. Gen.*, Feb. 20, 1926).

If the process be not arrested, death may result from the extension of the local infection to some vital organ, as the brain or peritoneum.

In pregnant women, erysipelas, in the majority of cases, does not cause abortion. If confinement or miscarriage occur during its course, there is no genital infection, provided obstetrical antisepsis be rigorously practised; moreover, the children at birth, according to Le Gendre, show no trace of erysipelas.

Synovitis or suppurative arthritis may occur as a complication of erysipelas. In 817 cases of erysipelas recorded by Gamgee one or the other of these conditions took place. The complication may arise at any time during the attack. The suppurative form requires the promptest and most heroic treatment. Disorganization of the joint will follow, even the death of the patient, otherwise. Furuncles may follow an attack of erysipelas.

In a single case, Zeller and Arnold observed, in the course of a year and a quarter, about 650 furuncles, affecting all parts of the body, including the hairy scalp. Fever, up to 100° F.



and more, but without distinct relation to the abscess formation, was observed. There was little depression of the general health, and the termination was complete cure.

The kidneys, according to Pollatscheck, are affected in about 38 per cent. of all cases. This is evidenced in the kidneys by the presence of casts with or without albumin, of albumin with or without casts, or of both. The presence of even large quantities of albumin with renal elements in the sediment may be only transitory, and does not necessarily imply an unfavorable prognosis.

Renal complications are to be expected with erysipelas. Of 483 reports of cases examined, 327 (67.7 per cent.) had excreted pathological urine. The mortality, however, did not apparently indicate that it was a very serious complication. In 66 of the cases the erysipelas was limited in extent; in 486 it was extensive. The scalp was primarily involved in 12 cases, but of the 485 cases beginning in the face in only 7 did the disease extend beyond the hair margin, the scalp remaining unaffected. Glycosuria occurred in a certain percentage of the cases. Boston and Blackburn (*Jour. Amer. Med. Assoc.*, Nov. 2, 1907).

Death may result from exhaustion consequent upon the febrile process and weakening of the organs by gradual infection.

The duration of the infection is very uncertain. It may seem to have disappeared, and subsequently starts up again. It may last a few hours, and continue for several weeks. Again, it may travel over the whole body and possibly attack the same locality several times. As a rule, it delineates its course within two or three weeks.

Examination of the blood, whether made during an attack or during the period of convalescence, as emphasized by Chantemesse, furnishes valuable information regarding the course of an attack of erysipelas. The curve of the number of leucocytes in a case of erysipelas follows very closely that of the temperature, but this leucocytosis does not show equally throughout the various blood elements. The polynucleated cells show an increase as soon as the malady is established, while at the same time the number of mononucleated cells diminishes, such diminution occurring chiefly in the lymphocytes. When recovery takes place it is signalized by a fall in the number of polynucleated cells. The eosinophile cells, which fell in number during the course of the illness, only appear again when the blood infection is altogether at an end.

In at least one-third of cases of severe erysipelas the blood yields a pure culture of the streptococcus. Such a finding does not, however, imply an unfavorable prognosis. Streptococcic septicemia in a small proportion of cases and pyemia almost always may become complicated with infectious endocarditis. This involves the left side of the heart, particularly the mitral valve, which becomes covered with small vegetations. It is often overlooked, since generally there are no physical signs, though there is always a possibility of multiple embolism. Abnormal sounds heard over the precordium in erysipelas are only in exceptional instances due to endocarditis. Lesné, Françon and Gérard (*Presse méd.*, Sept. 14, 1912).

Some persons are subject to "habitual attacks" of erysipelas, generally about the face, and probably repeated infections from a chronic nasal catarrh. As well shown by the

researches of Christian C. Holmes (1907) the pneumococcus and streptococcus are the two principal pathogenic bacteria which have their normal habitat in the nose and accessory sinuses. Hence the relatively frequent occurrence of facial erysipelas with a primary infection in these cavities. In most instances, according to Lavrand, spontaneous recurrent erysipelas of the face develops from the nasal fossæ through the lachrymal duct or the nostrils. The point of departure is either in the nasal fossæ or, more frequently, in the more or less hypertrophied adenoid tissue of the pharyngeal cavity.

Erysipelas has no appreciable influence on the duration and amount of the menstrual flow. On the contrary, according to Salvy, menstruation favors the development of erysipelas. Recurrences during the flow are due to the peculiar nervous state of the patient and to the persistence of colonies of streptococci in the skin and lymph-spaces, whose virulence has not been entirely destroyed.

Case which is of interest on account of the presence of a mastoiditis during an attack of erysipelas. An operation was urgently demanded. In spite of the fact that such an operation was done within the erysipelatous area, not the slightest disturbance in the way of any serious complication occurred. Wiener (*Med. Rec.*, Oct. 22, 1910).

Erysipelas of the larynx is more common than is generally supposed, though the literature does not indicate that the condition has been frequently met with or studied to any great extent. Some difficulty is occasionally encountered in making a differential diagnosis, for, while the local phenomena are generally very different from some conditions of the throat, as tonsillitis, they cannot

always be distinguished from those of simple inflammation; and where only redness of the throat exists, it may be necessary to await the skin manifestations before a positive diagnosis can be made. The presence of phlyctenulæ in the throat makes the diagnosis less difficult, but adds to the gravity of the case, which may terminate even in gangrene.

The writer presents short histories of 3 cases, which show the seriousness of the condition and the necessity for early and energetic treatment. One case with a negative previous history became insane a few weeks after being discharged from the hospital cured, the mental derangement undoubtedly being due to the severe infection. D. Bryson Delavan (*Laryngoscope*, Mar., 1911).

Certain attacks of erysipelas have proved a source of immunity against anthrax, at least for a few days. There is a growing opinion that it exercises a direct effect against the development of sarcoma. Indeed, cases are reported of sarcomatous growths having gradually disappeared after an attack of purulent erysipelas; hence the practice of inoculating erysipelas in those suffering with inoperable sarcoma. This procedure is not, however, without danger to the patient, for it is not always possible to limit the development of the disease; hence the patient should be made cognizant of the risk to be run by the inoculation of erysipelas for the destruction of sarcoma.

In about a thousand cases of erysipelas, in over one-fourth of the number the affection was not recognized. Pure erysipelas is a mild, serous, and not a suppurative or destructive process; the patients should be protected against infections from other forms liable to superpose supuration and necrosis on the erysipelatous process. Phlegmons are par-

ticularly dangerous in this particular. Sorensen (Hospitalstidende, Jan. 13, 1913).

The diagnosis of ordinary erysipelas is very simple. Gradually increasing and spreading redness is characteristic, and it can only be mistaken for *erythema*. This latter infection, however, is not accompanied by fever, while erysipelas always is.

The following three signs are characteristic: 1. The sign of centrifugal maximum. The most marked lesions are always situated at a spot at some distance from the starting point on the periphery of the patch; so also are the swelling and pain on pressure. This sign is useful in distinguishing erysipelas from inflammatory troubles, dacryocystitis, dental abscess, parotiditis or mumps. 2. The ear sign. Owing to the close adherence of the dermis and perichondrium, and the absence of subcutaneous tissue in the ear, inflammatory processes stop short at the periphery, whereas erysipelas, being a dermatitis, spreads in the thickness of the skin itself, invading that of the ear as it does in any other part. 3. The pain sign. The erysipelatous patch is invariably exceedingly painful. The patient invariably makes a grimace and shrinks when it is pressed, whereas in acute eczema and ophthalmic zona the parts are not so tender on pressure. In dental abscess and dacryocystitis, however, the affections are both painful and tender, but in a different way. Milian (Progrès méd., No. 30, 1908).

**COMPLICATIONS.**—The wound may apparently not be interfered with in the healing process, while at the same time a deep cellulitis exists, and may finally end in suppuration. The open wound upon which erysipelas has developed will take a dry, gray, dirty, and glossy appearance, covered with a sort of croupous membrane, and will retain this appearance

until the intensity of the infection has disappeared. On the mucous membrane a swelled condition takes place, which may also cover itself with a croupous membrane. There may be marked disturbances of the central nervous system as the result of a high fever. Delirium and stupor, accompanied by vomiting and convulsions, may follow. A collapsed condition of the system may take place after the disappearance of the symptoms. Hallucinations and certain motor disturbances may occur. As a rule, the lymphatic glands are not affected in superficial erysipelas, while they may suppurate in a deeper form of the infection. Internal complications known as metastatic inflammations may take place. These may be septic bronchitis, pneumonia, or meningitis, while peritonitis may follow erysipelas of the neighboring parts. The local sequelæ of erysipelas are a thickened condition of the cellular tissue due to the obstruction of the lymphatic vessels and an impaired condition of the vitality of the skin, predisposing the parts to eczematous ulcerations. Deep cicatrices may also form as a permanent result.

**ETIOLOGY AND PATHOLOGY.**—Erysipelas is a violent inflammation of the lymph-channels, caused by the streptococcus. Although it is now generally conceded that the infectious agent, as described by Fehleisen as the cause of erysipelas, is identical with the streptococcus of suppuration, the symptoms of erysipelas are sufficiently different to warrant a description of this infection as a form of affection separate from ordinary suppuration. It has been proved that the virulence of the streptococcus varies materially with the

nature of the soil upon which it grows; that it will frequently acquire a greater virulence when the resistance of the subject is lessened, as in tuberculosis, diphtheria, scarlet fever, small-pox, typhoid fever, and influenza, and when the vitality of the body is reduced, as by overwork.

Case in which the pneumonia diplococcus was found in pure cultures in the exudate of the typical erysipelatous lesions on scalp and face. Crisis occurred on the seventh day. Connio (Riforma Med., July 14, 1917).

Erysipelas cannot be considered either a contagious or directly infectious disease; only patients who are particularly susceptible can contract the disease from others. Hays (N. Y. Med. Jour., Aug. 18, 1917).

The writers observed several instances of infection of other patients from erysipelas patients transferred to the internal clinic. They consider complete isolation necessary. Redlich and Krasso (Wiener klin. Woch., Mar. 11, 1926).

Its virulence materially differs in various animal organisms, as it is by no means equal to the virulence of the same streptococcus in mice or rabbits. Erysipelas can be produced in rabbits by the injection of the ordinary streptococcus of suppuration, and by that means acquire a greater virulence, and, if not attenuated, would reproduce symptoms of erysipelas in an ordinary wound infected with it. From its etiology, therefore, erysipelas is a non-specific disease, but is due to a higher state of virulence which the streptococcus happens to possess at the time it enters the tissues, or which it can soon acquire when the tissues are suited to its development in a virulent shape. It has also been demonstrated that erysipelas cocci may enter the blood; but, as a rule, they are not found in this fluid.

Erysipelas is an acute inflammation of the epidermis due to the presence of one of the organisms of the streptococcus class, of which the *Streptococcus pyogenes* is the most frequent example. Cellulitis appears to be a strictly comparable inflammation of the cellular tissues, and when the inflammatory processes involve both the epidermis and the cellular tissues the condition of cellulocutaneous erysipelas results. Acute lymphangitis would seem to be a less virulent infection, due, as a rule, to organisms of the staphylococcus class, with a greater tendency to spread, as its name implies, by the lymphatic system. Erysipelas is not, in the true sense of the term, a specific disease, since it may be produced by a variety of organisms, and these organisms are capable of producing other diseases. Panton and Adams (Lancet, Oct. 9, 1909).

Cold is a recognized etiological factor of erysipelas, doubtless owing to the weakened resistance of the skin to infection it entails. Hence the more frequent occurrence of the disease in cold weather and the influence of cold draughts in causing it.

Season has long been recognized as a prominent predisposing factor in erysipelas, the greatest number of cases, as shown by the histories of 564 cases, occurring during cold weather, and this is, in a measure, explained through the fact that men are more likely to suffer abrasions of the skin during the winter months. During June, July, August, and September, when in this climate we have our greatest heat, cases of erysipelas are few and, in fact, the rule is that during these months the erysipelas wards are often without a single occupant. Season also exerts a decided influence on the mortality rate, the greater proportionate number of deaths occurring during November, December, January, and February, at which months, in this climate, we

have our extreme cold. When the months of March and April are unusually cold the death rate is increased. Boston and Blackburn (Jour. Amer. Med. Assoc., Nov. 2, 1907).

**PROGNOSIS.**—The prognosis of erysipelas is very uncertain. The mortality rate is somewhat above 10 per cent. Much will depend upon the rapidity and intensity of the course of the infection, and upon the organs which may be secondarily invaded by the poison, or possibly a complication by which a septicemia may exist. Young and otherwise healthy persons would offer a favorable prognosis, while those more depleted, and especially those recovering from lingering disease, would offer less hope of recovery.

Age is of great clinical importance both as a predisposing and prognostic factor in erysipelas. In their series of 564 cases studied, the writers found all cases developing in children during the first year of life were followed by a fatal termination, while between the first and tenth years the disease was not fatal. At the other extreme of life the mortality rate in erysipelas is exceedingly high, 83 per cent. of cases terminating fatally in those after the age of 80, and 38 per cent. in those above the seventieth year. Possibly between the ages of 20 and 60 erysipelas is apt to represent a highly virulent type of infection, and complications develop early and are severe in character. In the senile the erysipelatous process is liable to be of a low grade of infection and to spread extensively. Of the 539 cases analyzed with reference to sex there were 342 males and 197 females, while of the 69 deaths 56 of them were males and 15 females. Boston and Blackburn (Jour. Amer. Med. Assoc., Nov. 2, 1907).

In 5270 cases of erysipelas at a hospital for women at Petrograd, the

total mortality was 4.4 per cent. but it was much higher with advancing years, being only 1 per cent. up to 20 and increasing progressively to 8 and 14 per cent. at 50, 60 and older. Ivanoff (Russky Vrach, xvi, No. 9, 1917).

**TREATMENT.**—**Local.**—The multiplicity of remedies advocated for the treatment of erysipelas is the best proof that no specific exists to arrest this infection.

Comparative results of various treatment employed in 71 cases of erysipelas. In 37 the writer used a combination of **camphor** and **chloral**, 1 part of the latter to 3 of the former, with good results. The patients all recovered, and, although the treatment did not appear to effect the course of the disease, the patients gained relief from the application. In 10 cases **ichthyol collodion** was used with equally good results. In 5 cases **application of cold water**, yielded good results, while in 5 other cases no treatment at all was given, except a little **calomel** and dilute **hydrochloric acid**; and the patients recovered just as quickly as did the others mentioned. In 3 cases every kind of treatment was tried, including the use of antistreptococcic serum, without avail. The patients died. **Red light** was tried in 3 cases. In the writer's opinion the treatment of erysipelas is expectant and there is no specific. Potter (Jour. Med. Soc. of N. J., June, 1907).

**Absolute alcohol** is one of the older remedies in which most confidence can be placed in cases in which the occlusive bandage can be applied with exactitude, as, for instance, in erysipelas of the extremities. It is more difficult to apply where the face is the part affected, but the writer was able by its use to bring to a standstill after twenty-four hours erysipelas of the face in an old woman 82 years of age. For erysipelas of the scalp it is very useful. Hecht (Therap. Monats., Jan., 1907).

The **hot-air douche** used in 19 cases of erysipelas caused rapid recovery.

The jet of superheated air was applied to the spot for half an hour to an hour two or three times a day. Absorption is promoted to such an extent that there is generally a slight rise of temperature afterward. The lesions were usually on the face and neck; when other parts of the body were involved a hot-air box or chamber or a hot flat-iron was used. Ritter (Münch. med. Woch., May 24, 1910).

An ointment composed of 1 part of **chlorinated lime** and 9 parts of **paraffin ointment** proved to be the best application in 15 cases treated, the temperature falling in two or three days, instead of in nine, as with other methods of treatment. C. Binz (Berl. klin. Woch., Nov. 1, 1909).

The writer has treated 77 cases of erysipelas differently localized, all serious and all occurring in women, with intramuscular injections of a 10 per cent. solution of **sodium nucleinate**, employing doses of 1, 2, or 3 c.c. (16, 32, or 48 minims). The injections were repeated every second or third day. They lowered the febrile temperature permanently after the first injection in half of the cases. M. E. Blumenau (Vratch, No. 45, 1911).

The application of antiseptics in erysipelas probably does not do more than prevent mixed infection. Among the antiseptics which may be used is **ichthyol** in ointment or aqueous solution of 10 to 50 per cent. strength, either painted on or applied thickly spread on lint or gauze, which should be changed frequently to prevent drying or sticking. Similarly, there may be applied gauze saturated with a solution of **phenol** (1 to 2 per cent.), **boric acid** (saturated solution), **picric acid** (1 per cent.), **sodium salicylate** (5 per cent.), **resorcinol** (2 to 5 per cent.), **mercury bichloride** (1:5000), **lead and opium wash**, **magnesium sulphate**, **alcohol**, or simply **cold water**. A bolder method is the injection of antiseptic solutions a little outside of the margin of the advancing inflammatory process, *e.g.*, a 2 per cent. solution of **phenol**, or solutions of the **bichloride** or **biniodide of mercury**.

The writer's favorite procedure in combating severe cases, however, is the continuous application of **ice** to the inflamed area. The parts are enveloped as thoroughly as possible, and where an extremity is involved it is placed in a trough of cracked ice for several days. A. P. Biddle (Jour. Mich. State Med. Soc., May, 1912).

Use of **buttermilk** advocated; it is to be applied on soft rags—buttercloth is excellent for the purpose—which are kept constantly wet with the remedy. F. S. Arnold (Practitioner, May, 1913).

The writer considers **ichthyol** still the best remedy for erysipelas. The ammonia contained in it contributes by producing a local anemia. In attempting to abort an early case **ichthyol** should be used externally and **ammonia** also given by the mouth. Unna (Deut. med. Woch., Nov. 10, 1921).

The writer treated successfully a case of severe erysipelas of the face in a baby aged 12 months by intramuscular injections of the father's **blood**. Three injections were made (into the buttock), of 15, 20 and 20 c.c., respectively. The blood was withdrawn from the cephalic vein of the father, and injected immediately, with a fresh needle, the blood having no time to clot. Pines (Brit. Med. Jour., Dec. 5, 1925).

A 5 per cent. solution of **mercurochrome-220 soluble** was applied to the affected area with cotton swabs, once daily, until the eruption was well on its way toward subsidence. In only 1 case did the affected area show any tendency to spread after the first application of the drug, and in this there was no spreading after the second application. Only 1 of the 8 cases treated with **mercurochrome** developed any complication, and this one not serious, while 2 of 3 cases treated by cold compresses developed serious complications. Eldridge (Annals of Clin. Med., Oct., 1925).

In 4 cases of erysipelas of the face, intramuscular injection of 5 to 10 c.c. of **cow's milk** the 2d, 3d or 4th day seemed to arrest the process at once,

and a second injection completed the cure. A. Jensen (*Ugeskrift f. Laeger*, Jan. 28, 1926).

Prevention, therefore, should be sought for. The greatest adherence to aseptic principles and in the subsequent dressings of the case will insure the impossibility of the wound's developing erysipelas. Should, however, a contaminated wound present itself with the developing disease, antisepsis must intelligently be applied to the particular case as our sheet-anchor. The various remedies advocated by different authors rest upon this principle, each only claiming his antiseptic to have given the best results. This is probably the case because the particular author has had most experience in his special method. Of all the antiseptics, one of those commonly believed to have the most germicidal power is 1:1000 **aqueous solution of mercuric chloride**, slightly acidified. The antiseptic must come in close proximity to the invading micro-organisms, in order that it should exert its destructive power. Any method which will facilitate this will fulfill the indications. I, therefore, believe, with Kunert, that multiple **scarifications** and **incisions** should be performed when possible in order to facilitate the direct absorption of the antiseptic solution, while I also advocate, with Riedel and Classen, the scarification of the advancing margins of the erysipelas, so as to cut the development across before the micro-organisms have had access to them and fill these developments with an antiseptic solution, and so destroy them as they advance. The parts are kept thoroughly irrigated with the **cold solution**. If the patient should have some idiosyn-

crazy against mercuric chloride, a 3 to 5 per cent. solution of **carbolic acid** may be used with efficiency. In fact, all the antiseptics known today have been, in turn, advocated, and, possibly, may be used with benefit.

Increase of virulence often occurs when infection is locked up in the subcutaneous tissues. The writer carried out experiments made to find whether or not it was possible to alter the virulence of staphylococci and streptococci so as to explain the clinical phenomena. He found that by taking a virulent strain of streptococcus and incubating it in an acid medium, the streptococcus changed to an apparently typical staphylococcus, while the same strain incubated in an alkaline or neutral medium retained streptococcic appearance and virulence. Earlier he had discovered that the acidifying of a bichloride of mercury solution would take away its action of coagulating the blood, thus rendering it more useful as an antiseptic application.

Applying these facts to the treatment of erysipelas, he used **acid ice-cold bichloride of mercury** solution locally in the treatment of this disease, making minute **scarifications**, especially for two or three inches beyond the infected area, so as to lie upon the lymphatic vessels. The venous capillary hemorrhage thus caused allows vast numbers of the infecting cocci to escape, and the ice-cold compress, kept wet with the solution and applied to the lymphatic vessels, helps to destroy those remaining. If the infection is deeper, involving the cellular tissue, an incision should be made over the infected area for thorough drainage and disinfection. If the nose or some delicate part of the face is involved the scarifications may be replaced by copious **acupuncture**. He has employed this method in a large number of cases, both in hospitals and private work, with unflinching success in checking from the first the start-

ing infection, and he believes that by this local treatment, in conjunction with the constitutional tonic treatment with tincture of chloride of iron, all the indications will be met. E. Laplace (Jour. Amer. Med. Assoc., July 20, 1907).

For erysipelas of the face and scalp **ichthyol** and **vaselin**, equal parts, form an excellent local application, placing over this absorbent cotton.

**Magnesium sulphate** in the form of saturated solution in water applied with compresses, kept constantly wet with the solution, and covered with oiled silk, has been found beneficial in a large number of cases.

Of the various remedies recommended for the treatment of erysipelas of the face **ichthyol** proved to be the most useful of all, applied in a mixture with equal parts of **traumaticine**. This was swabbed over the affected part three or four times a day, and the application was continued for forty-eight hours after all local symptoms had died out. **Ichthyol** may be used in many other ways, often to greater advantage. It may be applied pure, diluted with half its volume of boiled water, freely bathing the parts every day or twice a day. As it dries it forms a thick scab, thus rendering the use of successive dressings unnecessary. When all active symptoms have subsided it may be applied in an ointment. In the case of severe inflammation with oozing and suppuration it is better, for the first twenty-four or forty-eight hours, to apply dressings moistened with a 1 in 10 or 1 in 20 solution, applying the pure **ichthyol** at a later stage. In an ointment it is not so active and should be only used in cases with little inflammation:—

℞ *Ichthyolis* ..... ℥ss (2 Gm.).  
*Zinci oxidi*,  
*Adipis lanæ* ..... āā ℥ij (8 Gm.).  
*Paraffini mollis*  
 q. s. ad ..... ℥j (30 Gm.).  
 Misce. Fiat unguentum.

This is an excellent application when inflammation has disappeared. It should be used while redness persists, or the following cream may be substituted:—

℞ *Amyli* ..... ℥j (4 Gm.).  
*Zinci oxidi* ..... ℥ij (8 Gm.).  
*Adipis lanæ*,  
*Paraffini mollis* ..āā ℥ij (60 Gm.).  
*Liq. hydrogeni per-*  
*oxidi* ..... ℥ss (15 c.c.).  
 Misce. Fiat cremor.

Should any telangiectasis persist the following ointment will be found more effective:—

℞ *Sol. adrenalini chlori-*  
*ridi* (1:1000) .... ℥ss (2 Gm.).  
*Zinci oxidi*,  
*Adipis lanæ* ..... āā ℥ij (8 Gm.).  
*Paraffini mollis*  
 q. s. ad ..... ℥j (30 Gm.).  
 Misce. Fiat unguentum.

Castaigne and Fernet (Journal de méd. et chir. pratiques; Amer. Med., April, 1912).

A mixture of 1 part of **ichthyol** with 2 parts of **alcohol** gives prompt benefit when used locally. The preparation should be freely applied, after careful shaving of the hairy surfaces, until the involved areas and even the surrounding zone of healthy skin have acquired a dark-brown color. Dind (Revue méd. de la Suisse Romande, May, 1912).

The writer found that the application of **magnesium sulphate** solution was extremely beneficial. Pain and swelling abated, fever decreased, and extension of the disease was controlled in the majority of cases. Report of 72 cases of erysipelas treated by wet dressings of a saturated solution of magnesium sulphate in water as originally advocated by Lucker. He used it in 19 cases of erysipelas complicated with alcoholism, acute nephritis, myocarditis, pneumonia, etc., with but 3 deaths, and in 35 uncomplicated cases without a single death. This treatment has been applied by him and others to nearly 700 cases of various forms of inflamma-



tion with uniformly good results. Lucker claimed originally the following advantages for it: The patient promptly obtains relief from the distressing local symptoms. The temperature rapidly falls to normal, usually during the second twenty-four hours, thus eliminating possible complications from a more prolonged fever. There is no necessity for internal medication in uncomplicated cases, the only treatment being a milk diet until the temperature becomes normal. In the writer's own cases pain and swelling abated, fever decreased, and extension of the infection was controlled in all but 6 cases. Many of the cases were advanced and neglected, and consequently the results have not been so uniformly good as those reported by Lucker. In 6 cases the inflammatory process extended so rapidly that in spite of this treatment antistreptococcus serum was injected; only 1 of these cases recovered. Excluding the above and 7 moribund cases, there remained 59 cases, with 13 deaths and 46 recoveries, equivalent to about 22 per cent., as compared with about 16 per cent. in Lucker's complicated cases. Choksy (*Lancet*, Feb. 4, 1911).

The writer advocates strongly the local application of 10 per cent. **tincture of iodine** to the inflamed area and for several inches beyond it in all directions for the prompt control of erysipelas. He has used this remedy, thoroughly applied, in a very large number of cases and has found it far superior to any other which has been suggested. In many cases the temperature fell to normal and the constitutional symptoms began to subside within a comparatively few hours. The application must be most thorough, and where there are folds to be treated it is best to pour some of the iodine into them and spread it about with a cotton swab. In some cases a second application of tincture of iodine may be required, but in the majority one application will effectively check progress of the disease. Keppler (*Med. Klinik*, Dec. 31, 1916).

The writers have treated 5 cases of erysipelas with **tincture of iodine**. These were all limb cases. Not only was the involved area painted over but the entire limb was treated. The treatment was repeated 2 or 3 times each 24 hours and continued until 2 or 3 days after cessation of the infective manifestations.

Tincture of iodine is rapidly absorbed, and the healthy skin shows the brownish coloration which is an index of prolonged impregnation. The high temperature falls and there is rapid improvement of the general state. The spread of erysipelas is prevented. In no case was contagion to neighboring patients observed. Basset and Lechelle (*Bull. et mém. Soc. de chir. de Par.*, xlv, 1408, 1918).

The writer recommends **tincture of iodine**. An inch-wide ring is painted around the erysipelatous area, repeated in 5 minutes, and later renewed as soon as the brown color fades. This occurs quickly through the action of perspiration, but the skin must be kept perfectly dry, ointments being avoided. Although used years by the writer, this method, he states, has never disappointed him. Lammerhut (*Berl. klin. Woch.*, Nov. 21, 1921).

Hueter has recommended the parenchymatous injection of 2 or 3 per cent. solution of **carbolic acid** at the margin of the inflamed district, particularly in the beginning of erysipelas. It may also be painted over the erysipelatous area and washed off with **alcohol**.

In case of extension into the eyelids, where it is impractical to use the acid, Allen prescribes a **2 per cent. carbolic acid solution in unguentum hydrargyri ammoniati**, to be applied frequently.

The writer reports 82 cases of erysipelas treated by means of **carbolic acid** and **alcohol** during the past eight years. There were 67 complete remissions of symptoms in from twelve

hours to four days. There were 10 delayed recoveries, and the treatment failed in 5 of the cases. The technique of the method consists of painting with a swab of cotton the entire surface of the involved area, and extending about half an inch into the surrounding and apparently healthy skin, with a 95 per cent. solution of carbolic acid. This is left until the purplish color of the inflamed area is replaced by a pretty complete whitening of the skin. When large areas are involved, it is advisable that only a portion be painted at a time. The second step consists in going over the whitened areas very thoroughly with a second swab saturated with pure alcohol. Judd (*Med. Record*, vol. vii, p. 268, 1909).

Good results were obtained from **radiant light** in both mild and severe cases. A 50-candle power incandescent therapeutic lamp was used at a distance of 18 inches for 20 minutes every 2 to 3 hours. Next day there was visible just a fringe of erysipelatous "margin" at one spot. Next day there was no trace of erysipelas, though later a slight recrudescence was noted, dispelled by further treatment. L. B. Williams (*Amer. Jour. Electrotherap. and Radiol.*, Feb., 1917).

The writer had good results in erysipelas from the use of **picric acid** solution, 1 to 1000 with 12 Gm. (3 drams) of alcohol added to the quart (liter) of solution. The affected area is painted with the solution and a dry cotton dressing applied. This is repeated every 12 hours. Usually the eruption is checked in 3 days, with a rapid drop in temperature and general improvement in the patient's condition. Critzman (*Med. Standard*, Apr., 1917).

The writer found **brilliant green** efficient in 12 cases, the average time for subsidence of the attack being just over 5 days. There was no mortality in the series of 40 cases, but there was recurrence in 2 cases. He painted the affected area with a 5 per cent. aqueous solution once a day in mild cases and twice a day in severe

cases. A piece of lint is so adjusted as to prevent staining of bed-clothes. When the eruption has subsided discoloration can be removed in 3 or 4 days by vigorous washings, preferably with ether soap. J. E. Adams (*Brit. Med. Jour.*, Nov. 20, 1920).

In erysipelas spreading to the chest in infants, the writer witnessed encouraging effects from the use of the **quartz lamp**. After 2 treatments the condition was checked, and the high fever was abated after 2 or 3 days. Petényi (*Monats. f. Kinderheilk.*, June, 1921).

In cellulocutaneous erysipelas and cellulitis a series of **incisions**, each about two inches long, should be made in the inflamed cellular tissue in order to prevent gangrene and give exit to the pus or discharges. These incisions are made where the skin seems to be most inflamed, in the direction of the long axis of the limb, parallel with the blood-vessels, so that these shall not be wounded. It may be necessary to give an anesthetic to make these incisions.

**General Treatment.**—General treatment will essentially consist in feeding the patient and giving tonics; chief among these will be the tincture of the **chloride of iron** in doses of 30 drops every two hours. This is supposed to have more of a specific action than any other drug recommended for the purpose.

The best **diet** will be one based largely on milk and eggs.

The **bowels** should be **regulated**, and an **anodyne** given to induce sleep and relieve restlessness.

A number of Italian and Russian observers have reported beneficial results from the use of **diphtheria anti-toxin** in erysipelas.

Report of 7 cases of facial erysipelas treated with **diphtheria antitoxin**

injected subcutaneously and applied locally. The effects were eminently favorable. The writer used 10,500 units, giving 1500 by injections and the rest by local application. The last patient was a man of 50, and other measures were suspended after this treatment was commenced. Federici (*Gaz. degli Ospedali*, Oct. 20, 1907).

The writer witnessed a rapid fall of temperature with disappearance of the skin manifestations after the injection of ordinary **diphtheria anti-toxin**. In a few cases, a second injection was necessary to bring about the desired effect, while in a smaller percentage, usually of far-advanced cases, the serum was ineffective. Sometimes the symptoms of the disease itself disappear, but septic complications develop later. In other streptococcus infections, the serum was useless, so that it is as yet impossible to explain its action in erysipelas. O. Polak (*Wiener med. Woch.*, July 22, 1911).

**Vaccine therapy** has also an increasing number of advocates, but it is difficult at present to reach a final conclusion as to its actual value. (See also BACTERIAL VACCINES, in the second volume.)

Erysipelas has yielded so little to treatment in the past that it is not wholly strange that many medical men have abandoned therapeutic remedies, used supportive treatment and hoped for a living patient after the disease had "run its course"—i.e., developed sufficient specific resistance in the body to check further spread of the disease. The writers employed **bacterial treatment** in 3 cases of erysipelas, injecting dead streptococci with apparently uniformly good results. The dose in these cases varied from 30,000,000 to 60,000,000 dead **streptococci**. Duncan and Illman (*N. Y. Med. Jour.*, Sept. 19, 1909).

Series of 50 patients, treated with **erysipelas vaccine** showed that it is entirely unnecessary to prepare a

vaccine for each case. It is, however, advisable to have a composite stock vaccine derived from several different strains, from as many different cases. It is probable that the more virulent the case of erysipelas the more valuable will its streptococcus be as a vaccine. The method of treatment has been, in almost every case, to inoculate with 10,000,000 of the devitalized streptococci on the first visit if the case is a severe one, and with 20,000,000 if it is less severe. On the second day in the severe case the patient gets 10,000,000 more if there are signs of improvement. The most important of these signs is a certain clearing of the intellect, and the others are a lessened intensity of the local condition—less tenderness and pain. The temperature is not so satisfactory a guide, although a fall of two or three degrees on the morning following the injection is a valuable indication for a second inoculation. Ross and Johnson (*Jour. Amer. Med. Assoc.* Mar. 6, 1909).

**Vaccines**, both autogenous and polyvalent, have a decided and important place in the treatment of erysipelas. The writer treated 30 cases with a stock vaccine prepared from several patients, and to which was usually added a number of strains of streptococci obtained from various other virulent infections. In addition, this treatment was supplemented by autogenous preparations whenever possible. The first dose was given as soon as the diagnosis was evident, and followed after one or two days by a second, third, or fourth. Five or ten million organisms were usually given at first; later, ten or fifteen million.

The vaccines seemed decidedly to abbreviate the course of the disease. In several cases where the prognosis had been very grave, their use was followed by convalescence. The vaccines also promised much in the prevention of recurrent attacks; 3 of the 30 patients treated died, but in these the condition had been so desperate that no results could be expected.

In 3 cases in which there had been repeated recurrences up to the time of treatment, no further attacks occurred. W. H. Walters (Amer. Jour. of Dermat., July, 1912).

The use of **antistreptococcic serum** in the treatment is advocated by some observers and condemned by others. Its successful use, however, usually coincides with its early employment in a given case and with large doses. The effect of a successful serum injection is not manifested for twelve to twenty hours, and reaches its maximum in twenty-four hours.

Birkhaug (1926) has prepared an **erysipelas antistreptococci serum** which, in concentrated form, was given in doses of 15 to 20 c.c., with very favorable results, in sixty moderately severe cases. According to this observer, the cause of erysipelas is a specific type of *streptococcus hemolyticus*. Given early, the serum caused a critical fall of temperature and fading of the local lesion; in late cases, several injections were required.

All measures proved ineffectual until the writer began to give a subcutaneous injection every day of 50 c.c. of **antistreptococcus serum**. In very severe cases he gave an injection morning and evening. These doses were kept up for 2, 3 or 4 days; in one case for 5 days. In another case very severe erysipelas of the face, with much swelling, disappeared within 48 hours, after two injections of 60 c.c.. A **quinine** tonic is taken internally at the same time. There were no accidents from the serotherapy but quite frequently there was a serum rash, with pains in the joints, sometimes intense. These by-effects developed about five days after the last injection of serum. He injects 2 c.c. of the serum 4 hours before the main injection, to ward off any danger of anaphylaxis. Capitan (Bull. de l'Acad. de méd., May 22, 1917).

All the new-born with erysipelas at the Madrid Foundlings' Asylum having died, the writer succeeded in saving 3, and another in his private practice, by giving 3 or 4 injections of 10 c.c. of a **polyvalent antistreptococcus serum**. By the second injection the patches had blanched and their spread been arrested. He has found doses of 20 c.c. effectual also in older children. He also sprays or dresses the parts with 1 per thousand **mercuric chloride**, and has the infants breast fed. Briz (Siglo Medico, Apr. 13, 1918).

The writers used **diphtheria antitoxin intravenously** and obtained excellent results and better than those from **antistreptococcus serum**. They gave antitoxin only in the graver cases, with fever, delirium and prostration, but without abscesses. Three of forty-eight soldiers treated with the usual measures died, but none died when given this intravenous treatment. The dose was 10 c.c., representing 5000 units. Campani and Bergolli (Gaz. degli osped. e delle clin., Aug. 25, 1918).

The writer reports 3 cases in infants cured by **local use of antistreptococcic serum**. Boissieric-Lacroix (Jour. de Méd. de Bordeaux, Jan. 25, 1922).

In all cases due to streptococcal infection the writer considers early injection of 40 or 50 c.c. of **antistreptococcic serum** of great value; it is to be repeated daily. Serum injections about the eruption are also deemed valuable by the writer, who has observed over 500 epidemic cases in 1 year. Inflammation yields readily to **hot fomentations**. He found erysipelas of the scrotum frequent in the poorer classes. Erian (Pract., May, 1922).

**Convalescent erysipelas serum** from patients with normal temperature at least 1 week was used by the writers in 18 cases in an average dose of 15 to 20 c.c. intramuscularly, with remarkable improvement in 13 cases. Jordan and Dustin (Jour. Amer. Med. Assoc., Mar. 15, 1924).

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**ERYTHEMA. — DEFINITION.—**

Erythema in itself simply denotes redness of the skin in which varying gradations of tint from yellowish red to violaceous red, darkish red, bluish red, or even blackish red are observed. As a disturbance of the functions of the skin it implies, on the one hand, various forms of hyperemia or active inflammation.

**SIMPLE ERYTHEMA.**—In this form there is a discoloration of the skin, varying in tint, size, and shape, and due to an abnormal flux of blood to the tissues without the presence of inflammation.

**Symptoms.**—The affection is transient, the coloring fading under pressure, and is caused by numerous internal and external agencies. It is instanced by the abnormal flushings and blushings, which are the expression of the varied feelings, such as anger, joy, and shame; it is also produced by disturbances of digestion due to indigestible foods, alcohol, drugs, or by various external injuries, as, for instance, the action of heat or cold, poisonous plants or drugs, or traumatism. The lesions produced vary from the slightest tint of red to a very dark color, and vary in shape from a round or oval to an irregular patch.

There is a definite clinical entity with skin lesions of the erythema group, purpura, erythema, urticaria, and angioneurotic edema, in which visceral lesions occur as the result of the same type of lesion. The most common of these manifestations are arthritis, gastrointestinal symptoms, hematuria, and various renal disturbances. The visceral disturbances occur unaccompanied by the skin lesions. The disease is due to some disturbance in the small blood-vessels, almost always focal, causing dilatation, diapedesis, and exudation. The ultimate cause is unknown. H. A. Christian (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 9, 1917).

**ERYTHEMA PUDORIS.**—This form bears considerable analogy to the above, but it is the expression of menstrual disturbances, pregnancy, climatic influences, and general disorders. The difference between this and the foregoing variety lies in the

cause. This latter affection is the result of some physical influence, and usually progresses as the patient ages. Chronic blushers belong to this category.

**ERYTHEMA VENINATUM.**—Certain mineral and vegetable substances also produce an erythema, but if the contact is prolonged actual inflammation takes place, and vesicles, pustules, or other symptoms may be observed. This form of erythema occupies the point of contact, and is manifested by a distinct, pinkish-red, irregular patch of small or large size, according to the amount of surface acted upon by the irritant. Mustard, cantharides, sulphur, strong soaps, ivy and other plants, acids, and many other drugs may be mentioned as some of the causes. This form of erythema usually persists for some time after the removal of the causative influence, and in cases in which the skin is delicate energetic treatment will be demanded.

**ERYTHEMA CALORICUM.**—Both heat and cold may give rise to erythema. That induced by heat is diffuse, and, although its disappearance follows immediately upon the withdrawal of the causal factor, it may persist for some time in fair skins, to be, in turn, followed by some degree of desquamation. Exposure to the actinic rays of the sun is the usual and greatest exciting cause, although it is observed in many persons who are obliged to work around stoves or machinery.

Cooks, stokers, and men or women who warm their limbs before the open grate present gyrate patterns and annular patches of redness (*Erythema ab igne*, Crocker). This condition generally disappears without leaving any trace, but there are cases in which the causative influence is often repeated; some degree of pigmentation is induced and may persist for long periods, if it is ever at all removed.

Four cases of reticulate erythema and pigmentation due to long continued exposure of the skin to heat; they were decidedly below the normal standard of health either as a result of previous illness, alcoholism, or old age. In 1 case the erythema occurred in the lower part of the back and was the result of the continued use of a hot-water bag. M. B. Hartzell (Jour. of Cutan. Dis., Aug., 1912).

Hammer refers to certain cases in which the action of the sun's rays disappear immediately upon entrance indoors, and speaks of these cases as not being influenced by the heat of a fire, but as being observed in winter as well as in summer. Cold exerts a similar influence upon certain subjects and is shown by a livid, bluish, or cyanotic appearance at the point of contact. Exposed for long periods pigmentation may be observed, or the condition may terminate in inflammation or ulceration.

**ERYTHEMA TRAUMATICUM.**—Violence of slight degree causes a diffuse redness at the point of contact, which may vary from a slight tinge of yellowish red to that of a dark red. Even under slight traumatism, if contact is allowed to continue, the condition will induce inflammation with all its consequent phenomena of vesicles, pustules, or bullous lesions. Complications may arise in the form of a true dermatitis, eczema, or other form of irritation or ulceration, and permanent pigmentation follow.

The exciting agencies are numerous, and the degree of injury depends upon the actual cause. Ill-fitting wearing apparel or even bed-dressings, tight garters, shoes, trusses, and diapers are some of the factors most commonly met with, while feces and salivary and leucorrhœal discharges may represent another class among causal conditions.

There are at least four distinct types of eruptions involving the napkin region of infants, which are of non-syphilitic nature and which must be carefully distinguished from the eruptions of congenital syphilis. The most frequently occurring of these are the various forms of erythema of Jacquet: (1) Simple erythema is found oftenest on the prominent convex surfaces of the buttocks and neighboring parts; in severe cases it may extend to other parts of the body. It is most common in very young infants. (2) The erythemato-vesicular type presents in addition, toward the center of the convex area, small bright-red erosions; at the periphery of the erythematous areas are small vesicles; the erosions by coalescence denude large areas. (3) The erythemato-papular type has flat,

red papules on an erythematous base.

(4) In the ulcerating form the erosions have gone deeper instead of granulating. The last three forms occur in infants several months old. These four forms depend upon a vasomotor disturbance, possibly of gastrointestinal toxic origin, with a determining factor of local mechanical irritation. The seborrheic dermatitis occurs in babies a few months old. The entire napkin region is involved. The eruption is bright red, small scales being over all. Other parts besides the napkin region are also involved, more particularly the scalp, umbilicus, behind the ear, etc. The cause of the condition is microbic and the cure a daily boric acid bath, with sulphur ointment (10 grains to the ounce). A third class of eruptions is the vacciniform ecthyma; it resembles the erosive and ulcerative stage of Jacquet's erythema, and is of streptococcic origin. The bullous impetigo is also streptococcic. It is usually found in other parts of the body besides the napkin region. The phlyctenular margins reveal the impetiginous nature of the bullæ denuded of their epidermis. H. G. Adamson (*Brit. Jour. Dermat.*, vol. xxi, p. 37, 1909).

Repeated attacks leave the point of affection prone to other affections; the most important of these is bed-sore, which occurs as the result of being too long in one position and thus inducing pressure upon one portion of the body, or lying upon rough and unclean bed-linen. Certain occupations tend to the production of local erythema, as, for instance, in the case of persons who are obliged to remain seated for long periods, as shoemakers, or those who stand indefinitely, as clerks.

**ERYTHEMA NEONATORUM.**—During the first week of life we sometimes meet with a diffuse universal redness; according to Elliot, this rarely extends beyond the seventh day. Beginning as a pale-red spot, it reaches its highest coloration about the third or fourth day, and then gradually fades, without leaving any desquamation. Elliot states that "during its involution, a yellow color, resembling that of icterus, may

become apparent, and in very severe cases there may be petechia." The usual causal factor in its production is some form of external irritation, harsh manipulation, either with the hands or towel while bathing or dressing, and exposure to the atmosphere.

**ERYTHEMA LAËVE.**—This term is applied to red patches apparently produced by edematous conditions of the limbs; impaired circulation is the probable cause. Swelling, redness, tensity, and a glossy or waxy appearance of the skin are the usual symptoms met with. Allowed to continue, these symptoms usually terminate in ulceration. Erythema edematosum is applied when great edema is present.

**ERYTHEMA SIMPLEX SYMPTOMATICUM.**—Under this heading belong all the erythemas which are due to some internal derangement, whether of the intestinal canal or from some general disease of the system. In some instances the cause is the ingestion of some food which retards digestion; in others the general economy is disturbed by some drug, such as alcohol, phenacetin, or other substance. This form of erythema does not respect any portion of the body; it most frequently attacks the face, neck, and upper portion of the chest and back.

**ERYTHEMA INFANTILIS.**—Erythema in the infant results from derangements of digestion, teething, and a number of other affections to which young children are prone. It appears, for the most part, upon the face and trunk, although other surfaces are liable to be affected. It may vary from a rosy-red macule of diminutive size to a lesion circular or semicircular in form, or present multiform manifestations. It is rarely elevated, causes some itching, but usually disappears in a few days. It may be persistent if its causes are not removed, and is sometimes followed by a slight desquamation.

Case of a child under 2 years of age in whom death followed an erythematous eruption secondary to intestinal catarrh. Nuwin and Eddowes (Brit. Med. Jour., Feb. 3, 1912).

**ERYTHEMA MEDICAMENTOSUM.**—The lesions produced by drugs internally administered upon the skin are manifold in character and may at times resemble many other diseases of the skin, but the fact that one of a series of eruption-producing drugs—such

as the coal-tar derivatives, antipyrin, antifebrin, phenacetin, and others—as salicylic acid, quinine, and iodine—has been ingested will generally lead to a correct solution of the difficulty. (See DERMATITIS and the various drugs named).

Case of a man of 37 who had taken moderate doses of Fowler's solution for furunculosis during almost six weeks, when an eruption appeared on his hands, feet, thighs, and scrotum. Large bullæ formed upon an erythema, and crusts were noted upon the scrotum. Neumann (Wiener klin. Woch., Nov. 21, 1901).

Erythematous and urticarial rashes are usually of toxic origin, as witness their development in some individuals after taking certain articles of diet or drugs, or as the results of stings of insects or of nettles, or of contact with caterpillars of certain species. One must suppose, therefore, that the lesions of joints which accompany them are also due to toxic action. Garrod (Lancet, May 27, 1911).

**ANOMALOUS FORMS.**—Under this heading may be included forms mentioned by Duhring as occurring in the course of asthma, rheumatism, gout, hemiplegia, chorea, epilepsy, exophthalmic goiter, and other toxic influences.

Malaria may manifest itself as an eruptive disease, as noted by the writer in 62 out of 160 cases. The erythema varies in color from a bright pink to a pale pink or light lilac, and sometimes was universal, with the exception of the face, neck, soles, and palms. In its diffuse form it resembles the measles eruption, though generally paler, not involving the face or neck, and never becoming raised to form flattish papules. The macules are usually of the size of a rice grain or small lentil, though often smaller; are irregular in outline, and more or less confluent, being generally so grouped as to form irregularly crescentic figures. On the trunk the eruption is most marked on the lateral aspects of the thorax and abdomen. II. de Brun (Paris méd., Aug. 11, 1917).

This variety also includes the form observed during variola. It may be noticed about the second day of small-pox, and before the appearance of the specific eruption. According to Atkinson, of Baltimore, it generally spares the portions usually invaded by small-pox and rarely lasts more than twenty-four hours. The character of erythema observed is a diffuse redness, of a violaceous color, and in size varies from a pinhead to a Lima bean.

Measles is often confounded, both by parents and medical men, with rubeola and also with certain roseolas. Also there are erythemas which resemble the exanthem of measles and which are of gastrointestinal origin. In a healthy infant an eruption may suddenly appear, beginning, as in measles, on the neck. It may also occur on the trunk. There is no fever, malaise, or catarrh. There is, however, gastric disturbance, loss of appetite, furred tongue, fetid breath, and sometimes diarrhea. The writer draws attention to the importance of recognizing this condition in epidemics of measles, when a wrong diagnosis may be easily made. Raymond (*Jour. des Mal. Cutan. et Syph.*, Nov., 1903).

*Erythema vaccinum* occurs during the course of vaccination. It may appear early, during the first two days, or may be delayed until the sixth or seventh, or at the time of beginning ulceration. Many patches of macules may be found over the body surface, with here and there an isolated macule of a bright-red color.

*Erythema diphtheriticum* is the form of disease observed in connection with diphtheria, in both mild and severe cases. (See DIPHTHERIA.) It appears sometimes as late as the second or third day of the diphtheritic process, and may occupy the trunk or extremities only, or may cover the greater portion of the body. The lesions are a diffuse redness of a mottled, punctate, or scarlatiniform form, and when in patches it is generally located upon the thorax and abdomen, though frequently upon the extremities. According to A. R. Robinson, it does not usually increase in size after the first few hours and disappears during the next

twenty-four or forty-eight hours without leaving any desquamation.

*Erythema Choleraicum*.—According to Dühring, there is an erythematous eruption observed in cholera patients. It occurs in polymorphous manifestations. These are usually macular, maculopapular, or papular, and are noted upon the dorsal surfaces of both the hands and feet, forearms, legs, face, and trunk. It may appear either at the beginning or termination of the disease and disappears in the form of a desquamation.

Erythema also occurs at times in *uremia*, *Bright's disease*, and *jaundice*. According to both Le Cronier Lancaster and H. Pye-Smith, lesions are observed. In uremia the lesions usually occur during the later stages of the disease and just shortly before the patient's death. They are at first erythematous, and in a few days become papular; fresh erythematous and papular lesions may afterward be observed at different stages of development over portions of the body. The lesions appear upon the extensor surfaces of the hands, forearms, and legs, and when numerous are noted upon all portions of the body, including the palms of the hands, soles of the feet, and mucous membranes, and are especially well developed upon the face. Upon the face they tend to become confluent and cause great disfiguration. They are bright red, and beyond a slight deepening of tint remain as noted for three or four days. They disappear either as flaky desquamations (often being as large as those noted in exfoliative dermatitis), hemorrhages being noted in the papules either during or previous to this stage, leaving a red, brawny, thickened skin; or it may become eczematous and terminate in the formation of crusts or in the formation of pustules and abscesses. Itching sometimes accompanies this condition.

**Pathology.**—The erythemas are the result of disorders of the vascular system and particularly those of the smaller vessels contained in the upper layers of the corium, and which radiate from there to the strata of the epidermis. Hyperemia is but an excess of blood propelled into the smaller capillaries through vasomotor action. The hyperemia differs with the character of the exciting agency. Transitory hyperemia caused by a slight injury generally fades



quickly and no trace of its existence can afterward be determined, while those due to more marked lesions fade less quickly. Pressure leaves no visible change, though less pliability may be noticed. At first, in the active hyperemias, the skin may be of a lighter hue, but in passive hyperemia it becomes darker. Although the temperature is somewhat above that of the normal, it may not even effect or may even be slightly below that of the natural state.

**Prognosis.**—The prognosis of simple erythema is usually favorable. A slight hyperemic process, unaccompanied by inflammation, quickly subsides, although some degree of pigmentation may remain to mark its site.

**Treatment.**—When simple erythema is likely to disappear spontaneously, it is hardly necessary to advise any form of treatment, but in protracted cases, as well as those attended by recurrence, active measures should be resorted to. **Dietetic errors** should be **corrected**. Any intestinal irritant should be promptly removed by **cathartics**.

Rashes in children due to gastrointestinal disorders usually yield to fractional doses of **calomel**. In cases attended by tingling and burning or where a slight degree of exudation has taken place the application of some bland powder, simple lotion, or unguent will easily mend matters. **Boric acid**, either as a plain powder, in full or diluted strengths, a lotion in half or full saturated **solutions**, or as an **ointment**,  $\frac{1}{2}$  dram (2 Gm.) of **boric acid** to the ounce (30 c.c.) of ordinary **petrolatum**, will usually suffice. **Lycopodium** or **fullers' earth** will serve a similar purpose. At times it may be advisable to add a slight quantity of **carbolic acid** to procure early relief.

Schamberg recommends the following cooling lotion:—

**R** *Acidi carbolici* .....  $\pi$ xxx (2 c.c.).  
*Acidi borici* ..... 3j (4 Gm.).  
*Glycerini* ..... f3ij (8 c.c.).  
*Pulv. zinci oxidi* ..... 3j (4 Gm.).  
*Aquæ* ..... q. s. ad f3vj (180 c.c.).

M.

## ERYTHEMA SCARLATINIFORME.

—Erythema scarlatiniforme (named by Hardy), roseola scarlatiniforme (Bazin), or erythema scarlatinoides (Besnier), is an

erythematous skin eruption closely resembling that observed in scarlatina, and from which affection it must be differentiated.

The writer's streptococcus vaccine can awaken an erythema resembling in every respect that of scarlet fever. As the streptococci are killed before the individuals are inoculated, the facts observed demonstrate for the first time the existence of a specific streptococcus toxin. The writer's experiences at Moscow with large numbers of children, showed that none of the other curative sera induce the production of the scarlatinal eruption, and still less the combination of sore throat, vomiting, raspberry tongue, etc., characteristic of scarlet fever, which follow inoculation with the streptococcus vaccine. The "vaccination scarlet fever" is distinguished from true scarlet fever by its milder and more rapid course and by the absence of contagion to other individuals. Gabritschewsky (Berl. klin. Woch., Bd. xliv, No. 18, 1907).

**Symptoms.**—According to French dermatologists, there are two types of this affection. The one "érythème scarlatinoïde," an acute rash resembling either scarlatina or measles, and accompanied or not by desquamation; other "érythème desquamatif scarlatiniforme récidivant," a subacute erythematous outbreak, resembling very closely scarlatina, usually accompanied by desquamation. As its name implies, it is a recurrent affection.

In the more acute type the lesions may be preceded, from a few hours or two or three days, by some constitutional disturbance, notably malaise, with chilly sensation and a rise of temperature of two or three degrees. The lesions, which are of a pinkish-red or crimson color, are punctate or diffuse and situated on the chest, thighs, face, neck, and other regions, although they are not particular to any region. At times there may be slight itching or burning. The duration varies from a few days to one or more weeks. Aggravated acute types may desquamate either as thin, flaky scales or in large-sized exfoliations. Observers refer to still another type in which the affection simulates more particularly these characters of rubeola.

In addition to the general malaise, subacute cases are likely to present some disturbance of the renal functions and albuminuria. The lesions are rather more lasting and exist from periods varying from three to six weeks. When the eruption reaches its height there may be a lowering of the fever. A marked symptom of this variety is the number of recurrences, while desquamation is a prominent character. Hartzell refers to the diminution of severity with each succeeding attack.

**Diagnosis.**—Owing to the great resemblance of this affection to the rash of scarlatina, it is important that a close differentiation be obtained. The symptoms of the latter affection may present characters—such as the strawberry tongue, sore throat, great depression, and the presence of large or small quantities of albumin in the urine—which will usually be sufficient for all practical purposes.

The early desquamation or the desquamation during the height of the fever will generally serve to establish the nature of the affection present.

**Etiology.**—It may be the expression of forms of stomachic disturbances, such as produced by the ingestion of toxic agents, as alcohol, antipyrin, belladonna, copaiba, arsenic, opium, the iodides, salicylates, or carbolic acid.

Typhoid fever, surgical operations, rheumatism, parturition, certain infectious affections, and sewer-gas poisoning (Crocker) are among the numerous conditions which may give rise to the disease.

**Pathology.**—Why so many different avenues should lead to the same result is difficult to determine. Idiosyncrasy may play a very important part in assisting its appearance. Brocq has advanced the idea that the desquamative or subacute variety, as previously noted, is only a benign form of pityriasis rubra, but this theory has not obtained many followers.

**Prognosis.**—Serious consequences are unlikely to follow if produced by some form of irritative ingesta. Elliot states that the affection "is grave and indicative of death when it appears in the course of a pyemia, a septicemia, or a puerperal peritonitis." The relapses may be more or less numerous and a different cause may be ascertained in some cases for each recurrence.

**Treatment.**—The first indication is the removal of the inducing cause where possible. Should this be some form of irritative ingesta the use of **catharsis**, especially salines, may suffice. The local symptoms should be relieved by means of antipruritic or stimulating washes. **Boric and carbolic acids** (Schamberg's lotion for erythema simplex, *vide supra*) are probably the best remedies of this class. It may be deemed advisable in many cases to use more active local measures. For this purpose some active drugs, such as **menthol** or **thymol**, may be used.

Cases of erythema scarlatiniforme superposed on typhoid fever, show marked improvement under **epinephrin**, while conditions became aggravated whenever the epinephrin was suspended. Hutinel gives from 6 to 10 drops a day of the 1:1000 solution. In 1 case he kept up this dosage for several weeks with benefit and without by-effects. If it does not seem to be benefiting the child, he soon drops it.

Case of typhoid fever in a boy of 12 years, who presented a scarlatiniform erythema on the knees, elbows, and buttocks, besides a leaden tint, a bad facies, ulcerated lips and nostrils, congestion at base of left lung, delirium alternating with extreme prostration, a very grave case in fact, contrary to the run of cases in children, which are generally favorable. The treatment was **cold baths** (32° C. —89.6° F.), every three hours, **cold compresses** on the abdomen, **hypodermic injections of camphorated oil**, and every day a dose of **adrenalin**, 1:1000, 8 drops divided into two doses. Even Hippocrates knew the danger of erythematous eruption in the course of an infectious fever, but its gravity has escaped the attention of many modern pathologists. It may be morbilliform or scarlatiniform in character and is usually accompanied by the excoriation of lips or nostrils, a lesion which will infect the skin of the finger if the patient touches it. Great prostration and adynamia are characteristic and death is the usual termination. Similar erythemata appear in the course of other infections and are always a grave sign. They

must not be confounded with drug rashes. The autopsy in such cases discloses an enlarged liver with fatty degeneration; the renal system is also affected; the heart is often soft and discolored; the suprarenal capsules are enlarged and increased in weight; occasionally the thyroid and the pancreas are also altered. Fortunately adrenalin had a marvellous influence in the case under discussion; its remission was marked by a recrudescence of the symptoms, its renewal by their removal. It may be given for several weeks without danger, but should be watched. Hutinel (*Presse méd.*, March 13, 1912).

**ERYTHEMA INDURATUM SCROFULOSORUM.**—This condition was first described by Bazin under the title "érythème induré des scrofuleux." It is an affection that may be mistaken for erythema nodosum. It is found in those persons of strumous diathesis and especially women and young girls (Crocker) who are easily fatigued and who are obliged to remain for long periods in a standing position.

It generally presents itself upon the anterior surface of the legs and occasionally upon the calf (Crocker); the lesions may be deep-seated nodes or nodules, which are either absorbed or break down into suppurating ulcers. In color they are first of a bright red, but they soon become darker or of a livid tint. After breaking they are observed to be punched out, round or irregularly oval ulcerations which resemble to a marked extent gummatous lesions.

In differentiating the early characters from erythema nodosum the acute and shorter course observed in the latter affection is to be noted. It may usually be identified by means of the tuberculin test.

Case of erythema induratum of Bazin in a young woman aged 17 years. Her family history was negative with regard to tuberculosis. The patient was a healthy-looking young woman. Since childhood she had suffered from a weak peripheral circulation and chilblains. The characteristic lesions of Bazin's disease were present on both legs.

On March 19, 1909, an injection of  $\frac{1}{10}$  mgm. of the old tuberculin was

given, and as a result of this a slight general reaction occurred but no local reaction. Two days later an injection of  $\frac{7}{10}$  mgm. was given, which was followed by a marked general reaction and a local change, consisting of swelling, edema, and redness of the lesions. Some days later, at the site of the injections on the arm, two red, painful swellings about the size of five-mark pieces developed. These gradually disappeared, leaving pigmentation.

The histological appearance showed that the affection was essentially a vascular lesion. The vessels were dilated and surrounded by a cellular infiltration. In places the endothelium had proliferated and a thrombosis was observed. Considerable numbers of giant-cells were present, and in places caseation and necrotic changes were noted. G. A. Gavazzeni (*Monats. f. prakt. Derm.*, Sept., 1909).

Diagnosis from syphilitic gumma is established by its longer duration before the occurrence of ulceration, and the serpiginous outline of the latter, or the presence of scars.

**Treatment.**—The treatment is that of struma: **tonics, codliver oil, nutritious food, and out-of-door life.** Small doses of **thyroid gland**, not more than 1 grain (0.065 Gm.) three times daily in an adult may prove helpful. Where prolonged standing cannot be avoided, a well-applied **bandage** should be worn.

**ERYTHEMA EXUDATIVUM MULTIFORME.**—Erythema exudativum multiforme is an acute inflammatory and exudative affection of the skin, characterized by the appearance of macules, papules, or vesicles, discrete or confluent, and of varying sizes and configurations.

**Symptoms.**—The character of lesion observed, with its many configurations, has given rise to the use of certain terms which are indicative of the condition present: **erythema multiforme papulosum** is used when the predominating lesion is of the papular type; **erythema multiforme tuberculosum** when the size of lesion is slightly greater than the papule; **erythema multiforme vesiculosum** when of the vesicular type;

*erythema multiforme bullosum* when bullous; *erythema multiforme annulare seu circinatum* when it assumes an annular or rounded form; *erythema multiforme figuratum seu gyratum* when peculiar irregular lesions are formed from a coalescence of two or more annular or circinate rings; *erythema multiforme iris* when new lesions appear successively in the clearing center of preceding manifestation; *erythema multiforme vesiculosum circinatum* (*herpes circinatus*) when the borders of a papule are covered with a ring of vesicles; *erythema multiforme vesiculosum iris* (*herpes iris*) when several concentric rings of vesicles are formed; *erythema multiforme urticatum* (*lichen urticatus*) when from the edema they closely resemble urticaria.

In Osler's group of 29 cases of *erythema multiforme* with visceral lesions, the number of symptoms present in any given case varied between four and ten. Purpura was noted in 22 cases, urticaria in 17 cases, edema in 5 cases, *erythema* in 14 cases, fever in 14 cases, colic in 25 cases, vomiting in 15 cases, diarrhea in 5 cases, hemorrhages in 14 cases, nephritis in 14 cases, albuminuria in 15 cases, arthralgic pains in 17 cases, endocarditis in 3 cases, and enlarged spleen in 3 cases. Various other manifestations were noted in one or two cases only. In the first case there were edema, *erythema*, fever, colic, vomiting, hemorrhages (from the kidneys), nephritis (including the albuminuria, classified separately in Osler's article), arthralgic pains, and enlarged spleen; in the second case, purpura, edema, *erythema*, fever, hemorrhage, arthralgic pains, and the group of symptoms relating to the nervous system, coma, hyperesthesia, photophobia, etc. Hall (Boston Med. and Surg. Jour., Sept. 3, 1908).

*Erythema exudativum multiforme* has points of predilection. For the most part lesions are observed upon the backs of the hands and feet, the forearms, and the legs. Next in frequency they occur upon the region of the head, the cheeks and neck, and lastly upon the trunk, the chest and back, and the abdomen. In aggravated

cases, or in those unusual types, the lesions may be observed in other parts of the surface. They are usually first noted upon the hands and fingers, and from these regions spread to other parts, and result in some cases (as recorded by Dühring) in an enormous involvement of the whole general surface.

Death has been observed by Vidal and Leloir, and Molencs-Mahon speaks of a number in which death also occurred.

*Appendicitis* as a visceral manifestation of *erythema exudativum multiforme* in 2 cases reported by the writer eight years ago. The matter of diagnosis is one of grave importance. The attack of colic, the so-called abdominal crisis of exudative *erythema*, may easily lead the inexperienced to make a diagnosis of *appendicitis* when no such lesion exists; on the other hand, a more serious mistake may be made of overlooking the coexisting appendix trouble, unless it is recognized that these vasomotor circulatory disturbances do at times result in congestion of, and even hemorrhage into, the appendix, with the result that there may be bacterial infection and inflammation or actual gangrene of this organ. Chenoweth (Med. News, March 4, 1905).

A girl of 18 suffered a frequently relapsing eruption thought to be *E. multiforme*. Steady deterioration and a severe anemia of secondary type developed. The liver and spleen became enlarged, also the axillary and inguinal lymph-glands. There was albuminuria. Blood culture yielded *Staphylococcus albus*. Facial erysipelas preceded death.

Kirschenblatt (Derm. Zeit., Feb., 1925).

**Diagnosis.**—The fact that death can occur from this affection renders an exact diagnosis of especial importance.

*Eczema.*—In papular *eczema* we may notice a symmetrical arrangement, but usually the lesions are regular as to size and outline. They may retain their appearance, but are prone to become either vesicles or pustules. Their duration is rather more lengthened, and crusting is likely to result from the excessive exudation.

*Psoriasis.*—*Psoriasis* is not likely to assume a symmetrical arrangement. It is more

likely to be covered with decided desquamations and to be of much longer duration.

*Tinea Circinata*.—Circinate ringworm is not usually symmetrical, is slower in its extension, and more persistent in its character. The edges in this affection are usually well defined.

*Syphilis*.—Careful examination should be sufficient to make a correct diagnosis. The papular and other varieties will usually give some distinct sign of syphilis.

*Urticaria*.—The lesions of urticaria are mostly uniform and of a white color, usually of short duration (rather evanescent) and are not likely to present different stages.

*Pemphigus*.—The lesions of pemphigus are bullous, always remain so, and depart as such, while they appear rapidly and are asymmetrical; they are not accompanied with much inflammation.

*Dermatitis Herpetiformis*.—In this affection the lesions are multiform (erythematous, vesicular, bullous, or pustular), are not symmetrical, and usually run a chronic course.

*Erythema Nodosum*.—The lesions are deep-seated and nodular, are usually observed upon the lower extremities (along the tibia), do not change in appearance, and are painful (almost rheumatiform) at all times.

**Etiology.**—The cause or causes of this affection are obscure. It presents a tendency to recur at certain seasons of the year (usually the spring and fall), and is probably influenced by climatic changes.

Numerous cases are recorded in which the affection recurred at regular intervals, as, for instance, every year at the same time, every three months, at intervals of six or more months, or at longer stated intervals. All ages are affected, and the disease seems more greatly to attack young children and young females. There is no doubt but that certain affections predispose to its appearance, *viz.*, rheumatism, gout, uremia, Bright's disease, jaundice, diphtheria, and cholera.

Case in which when pregnancy had been of a few weeks' duration there was a severe attack of erythema multiforme, the lesions in the early parts of the outbreaks being papular and erythematous, later of the iris form and vesicular, and finally bullous. This eruption persisted during four

entire pregnancies, and continued for from four to eight weeks *post partum*. Gotheil (Amer. Jour. of Obstet., April, 1910).

The writer refers to 14 cases of erythema multiforme complicating vaccination, 7 of which were seen by him. While definite conclusions as to the causative agent could not be made, the analogy between these eruptions and hemorrhagic smallpox was evident. The probable incidence of this type of eruption is estimated at approximately 1 in 10,000 vaccinations. Eichenlaub (So. Med. Jour., Mar., 1926).

Certain drugs taken internally may also be mentioned as a possible influence.

**Pathology.**—Erythema multiforme begins essentially as an hyperemia, and is quickly converted into an exudative inflammatory disorder. It can hardly be classed as an essential and specific disease, a fact which some authors claim if we can really believe that so many diverse conditions will produce it. There is no doubt but that we have in the process an angioneurotic element, as claimed by Schwimmer, Lewin, and Auspitz. Many others have observed microorganisms in the blood and lesions.

**Prognosis.**—All cases tend to rapid recovery, although a number of relapses may occur. Deaths have been recorded, but when the large number of cases is taken into consideration this loss of life is very small.

**Treatment.**—Internal treatment is to be directed toward the removal of the exciting cause where possible. All intestinal irregularities are to be remedied. Calomel is often efficacious as hepatic stimulant. Intestinal antiseptics such as salol, sodium salicylate and creosote carbonate are often helpful. Any tendency to rheumatism must receive attention, and potassium iodide, recommended by Villemin, may be found of good service, 15 to 30 grains (1 to 2 Gm.), thrice daily, as an absorbent in the vesicular and bullous form. Elliot says that it may, if given injudiciously, provoke an aggravation of existing conditions. In this class of cases, Atkinson, of Baltimore, relies upon salicylic acid and the salicylates. Cantrell frequently obtained excellent results with arsenic trioxide given during and between attacks.

Case of erythema multiforme, in a woman aged 27, that had existed from childhood, occurring every fall and disappearing in the winter. Intramuscular injections of  $\frac{3}{4}$  grain (0.048 Gm.) of **cacodylate of soda**, given twice a week for several weeks, completely relieved the attack. Each injection was followed by relief and the disease disappeared entirely, leaving her in better condition, according to her own statement, than she had ever been in since it first occurred. From his experience in this case the writer would recommend cacodylate of soda injections for trial in all cases of erythema, more especially in the angio-neurotic type. W. Cuthbertson (Jour. Amer. Med. Assoc., Jan. 6, 1912).

**Quinine** is certainly demanded in those types which are presumably the effect of malaria. Antistrumous remedies—such as **codliver oil**, **phosphorus**, and possibly **strychnine**—in those debilitated by such processes are valuable in the tubercular forms.

Local measures, while possibly directed alone to the relief of subjective symptoms, may also be found beneficial. **Boric acid** is of distinct value in this affection, and applied in a saturated watery solution gives almost instant relief from the itching and burning that are occasionally observed. Schamberg recommends the following as a sedative and antipruritic lotion:—

**R** *Resorcini* ..... 3j (4 Gm.).  
*Acidi borici* ..... 3j (4 Gm.).  
*Glycerini* ..... f3j (4 c.c.).  
*Zinci oxidi* ..... 3ij (8 Gm.).  
*Spirit. vini rect.* ..... f3j (30 c.c.).  
*Aquæ* ..... q. s. ad f3ij (60 c.c.).

M. Sig.: Apply frequently.

The **sulphite** or **hyposulphite of sodium** may often be used advantageously in the strength of from  $\frac{1}{2}$  to 1 dram (2 to 4 Gm.) to the ounce (30 c.c.) of water. **Ichthyol** may be found of service in the vesicular and bullous types. At times stimulating remedies may act efficaciously, especially **salicylic acid**, **carbolic acid**, and **sulphurous acid**, in varying strengths of solution.

In the urticarical type antipruritic lotions such as the above may be demanded. Mild

cases may not require treatment, the subjective symptoms being very slight.

Many striking illustrations of the beneficial effect of a restriction of nitrogenous food under certain conditions are found in the use of the so-called "**rice diet**," which included hot boiled rice and bread at least twenty-four hours old. In severe erythema multiforme, in various acute inflammatory affections, in recurrent vesicular eruptions of the hands, in some eczemas, in the acute exacerbations of psoriasis, and in severe rheumatoid arthritis, the "**rice diet**" caused a complete cessation of distressing symptoms and a disappearance of the lesions. L. Duncan Bulkley (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 15, 1912).

**ERYTHEMA NODOSUM.**—Erythema nodosum is an acute inflammatory affection of the skin, characterized by the appearance of symmetrical, elevated, variously sized, shaped, and colored nodular formations, accompanied by constitutional disturbance.

Evidence is accumulating that associated or subsequent tuberculous lesions bear a causal relation to the skin disease. Chauffard found a typical erythematous node develop at the point of injection of tuberculin in a tuberculous girl. Landouzy discovered a tubercle bacillus in cutting an erythematous node, and guinea-pigs inoculated with scraps from this node developed severe local and general tuberculosis. Jaquerod (Revue méd. de la Suisse rom., June, 1916).

From 1 insurance company, out of 46 cases with previous histories of erythema nodosum, the writer learned that 10 persons (3 males, 7 females) had later developed tuberculosis—21.7 per cent. The interval between the two conditions varied from  $2\frac{1}{2}$  months to 12 years. H. J. Vetlesen (Norsk Mag. f. Lægevidensk., Nov., 1924).

Erythema nodosum appears at the moment when the organism becomes allergic to tuberculosis. It represents a tuberculous eruption. A. Wallgren (Acta Paediatrica, Mar. 6, 1926).

**Symptoms.**—Preceding the appearance of the lesions of an erythema nodosum there is usually general constitutional disturbance. Chills, with an elevation of temperature, or myalgic or rheumatic pains may be encountered. Duhring pointed out that edema may be one of the first symptoms, while visceral involvement—with, later on, lesions of the heart and kidneys—may be present. For the most part, the nodes are localized upon the anterior surface of the shins, along the line of the tibiae, and are arranged symmetrically. They are also observed, in exceptional instances, upon other parts, the arms, face, and chest, along the line of the ribs, and upon the abdomen. Pospelow, quoted by Elliot, noted similar involvement of the mucous membrane of the mouth. These nodes appear rather suddenly, developing rapidly, and are of a light or rosy red color, but later become darker in appearance, of a bluish or of a purplish tint. Appearing either singly (usually) or in crops, the process may extend over a period of from one to five weeks (or longer), although each individual lesion lasts only about six or eight days. While disappearing they assume various colors, from a yellow to blue or purple, and closely resemble a bruise. During their height they have a tense and shiny look, and give to the touch an indistinct impression of containing fluid. They rarely suppurate, absorption generally taking place, although this result has been observed by Haisholt and others. Dilatation of the capillaries has been observed by Lewin and Unna, while Van Harlingen has noted lymphatic involvement. Hemorrhage has, according to Denime, been observed in a case in which gangrene also took place. They are always painful and at first are firm to the touch, although they soon become softer, as they are disappearing. Some authors have described an ominous form of the affection in which tuberculosis is noted. Occasionally erythema nodosum and erythema multiforme are co-existent, especially that variety of erythema multiforme in which papules are the predominating manifestation.

Erythema nodosum followed measles in 9 out of 300 cases. In most of the cases about ten to fourteen days had elapsed since the first onset of measles before the erythema nodosum

made its appearance. In half the cases the first symptom was pain in the joints, followed by the erythema in about twenty-four hours. There was no history of rheumatism or contact with rheumatic fever in any of the cases, and no rheumatic or cardiac lesions were found in any case. Joynt (Brit. Med. Jour., April 15, 1911).

**Diagnosis.**—While, with a careful survey of the lesions presented, as well as the concomitant phenomena, little cause may exist for diagnostic error, some instances do occur in which difficulty may be experienced.

*Contusions* are likely to be single and do not present the deep nodular formations. The cause can generally be determined.

*Syphilis.*—The syphilitic gummata, especially the non-ulcerating variety, which often resemble erythema nodosum, are sharply defined, indolent, and occasion no pain.

*Erysipelas* generally presents a hard, though diffuse, inflammation, instead of a more circumscribed character of swelling.

*Erythème induré des scrofuleux* is not painful, is asymmetrical, of longer duration, and tends to ulceration; it occurs in scrofulous subjects.

**Etiology.**—Erythema nodosum is an affection of early life, although instances in which it has affected varying ages have been recorded. Out of a total of 108 cases, S. Mackenzie found 14 under 10 years of age, 69 between 10 and 30, 15 between 30 and 40 years, and 10 over 40 years of age. Comby has presumably recorded the youngest, 14 months old. Most authors consider that the spring and autumn contribute the greatest number. Rheumatism accompanied many cases. Malaria was found to be a possible exciting cause by Boicesco.

Six cases of erythema nodosum with exudation affecting the mouth or upper air-passages, occurring in persons years after syphilitic infection. The latter probably merely afforded a predisposition to the lesion. Mercurial treatment is unnecessary. In the cases reported excellent results were obtained with **potassium iodide**, and in every instance there was a prompt and salutary reaction to **salicylic acid**. Trautmann (Munch. med. Woch., Bd. liii, Nu. 43, 1906).

The writer noted that the signs or history of chorea, endocarditis, or arthritis are not found in more than 10 per cent. of all cases of erythema nodosum. The disease differs from rheumatic fever further in that it more commonly attacks females than males, and is most prevalent in the autumn, winter, and spring, while rheumatism is most common in summer. A long period of prodromal malaise, comparative freedom from the risk of recurrence, slight constitutional disturbance during the pyrexial period, and the presence of phlyctenulae in the eyes are also characteristic of erythema nodosum. The arthritis may differ entirely from that met with in rheumatic fever, and it, together with the pyrexia and rash, are apparently only slightly influenced by the administration of salicylates. Symes (*Brit. Med. Jour.*, July 27, 1907).

Erythema nodosum was formerly classed among the rheumatic eruptions with erythema multiforme and rheumatoid purpura. These 2 conditions are now recognized as constituting 2 distinct and separate groups, and erythema nodosum has been shown to be a disease standing in some sort of relationship to an acute outbreak of pulmonary tuberculosis. Erythema nodosum occurs only in tuberculous subjects, usually in those in whom the infection is still latent. It is the outward and visible manifestation of slight, attenuated, curable tuberculosis, and is of bacillary origin. Experimental observation confirms this. The inoculation of fragments of the erythematous tissue in animals rendered them tuberculous, and the histological structure is that of typical "tubercles." The cuti-reaction is positive; an exactly similar nodule can be provoked by injecting a minute quantity of diluted tuberculin into the dermis. Erythema nodosum is, then, a bacilleamia which can, of course, be recovered from, but which is none the less an outbreak of bacillary infection, and must be treated as such. Marfan (*Med. Press*, July 3, 1918).

Basing his opinion on personal experience of about 100 cases, the writer contends that the disease is an acute specific fever. A prodromal stage with joint pains, languor, malaise, etc., occurs, the duration of which appears to average about 12 days. The author does not believe in a relationship to rheumatism, as salicylates have no effect, and there are never cardiac sequelæ. A. A. Lendon (*Brit. Med Jour.*, Apr. 4, 1925).

**Pathology.**—Erythema nodosum is due to an inflammatory process at first active and later passive. Atkinson, of Baltimore, argues that it is an overcrowding of blood- and lymph-vascular spaces and exudation of blood-cells, both white and red. The process affects the entire skin, and is believed by Kaposi to be a more fully developed and stable urticarial wheal.

**Prognosis.**—The prognosis is usually favorable. Relapses may occur or the process may be extended by successive outbreaks of new lesions. The usual length of each attack is from one to five weeks, although the individual lesions usually run their course in from six to eight days. Death has been recorded, but this is exceptionally rare.

**Treatment.**—The disease tends spontaneously toward recovery, and it is very highly probable that constitutional measures exert little influence. General disturbances of the constitution require appropriate attention. A bland diet should be advocated and rest in bed advised. Iron, quinine, phosphorus, acetanilide, and phenacetin are often beneficial. To reduce inflammation, relieve pain, and prevent complications, a solution of sulphite or the hyposulphite of sodium in water, 1 dram (4 Gm.) of either to the ounce (30 c.c.), will be found useful. Ichthyol has also been of service in many hands (1 dram—4 Gm.—to the pint—500 c.c.—of water). Phenol, sulphurous acid solutions, lead water and laudanum, boric acid, and hot fomentations may also be mentioned as useful remedies when the others fail.

The writers recommend rest in bed, with wet compresses of water, slightly alcoholic and covered with absorbent wool. If the pain is very severe, apply petrolatum 40 Gm. (1½ ounces), ex-



tract of **belladonna** 0.50 Gm. ( $7\frac{1}{2}$  grains), and extract of **opium** 0.25 Gm. (4 grains) as an ointment, and cover the limb. **Sodium salicylate** and **potassium iodide** are of value. If signs of tuberculosis are present, open-air treatment is advisable, with good food and hygienic conditions. Deléarde and Hallez (Brit. Med. Jour., Oct. 7, 1911).

In a case of erythema nodosum in a child of 28 months, in which the disease had followed whooping-cough and bronchopneumonia, scarlet fever also developed, the nodes appearing on the ninth day of the scarlatinal rash, and becoming purplish 2 days later. **Anti-streptococcal** (scarlatina) serum was injected intradermally into one of the nodules. A pale area was evident around the nodule and the case proceeded to recovery. Percival (Edinburgh Med. Jour., Nov., 1925).

C. and S.

**ERYTHROL TETRANITRATE** is a polyatomic organic nitrate which, as do all bodies of this class, detonates when struck with a hard body. In this particular it is even more sensitive than gun-cotton or dynamite. Its dangerous activity may be developed when gently stirred with apparently harmless compounds. An explosion of erythrol tetranitrate cost Mr Lewis Jones, a qualified chemist, his life, while engaged in stirring together in a mortar a mixture of erythrol tetranitrate and lactose. The quantity of the active drug served out to him was 4 ounces.

Bradbury holds that the drug is perfectly safe unless rapidly heated or struck or mixed with some readily oxidizable body.

Erythrol tetranitrate is solid and crystalline, and melts at a temperature of  $61^{\circ}$  C. ( $142^{\circ}$  F.). When pure it is colorless, and if kept in a dark and moderately cool place is fairly stable. If exposed to warmth, and especially sunlight, it rapidly undergoes decomposition, turning yellow and giving off nitrous fumes.

**PREPARATIONS AND DOSE.**—The dose of the solid nitrate is  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 Gm.). It can be given in pill, tablets, or in alcoholic solution. Its solubility in water is slight, but it dissolves readily in alcohol and in ether.

**PHYSIOLOGICAL ACTION.**—It is a vasodilator, and belongs to the group of which glyceryl trinitrate, known familiarly as nitroglycerin, may be regarded as the typical representative. Its action is slower and more lasting than that of nitroglycerin, beginning in about fifteen minutes and lasting for three to four hours. Blood-pressure experiments show that the nitrates of erythrol and mannitol have a less marked, but more prolonged, action than glycerol and glycol.

**THERAPEUTICS.**—Bradbury speaks highly of its therapeutic properties in warding off attacks of **angina pectoris** and in keeping down arterial tension in chronic **Bright's disease**. In the former disease it is sometimes necessary, to avert the paroxysms, to administer the remedy in steadily increasing doses. Garaway treated a case in which the patient finally took  $\frac{1}{2}$  dram (2 Gm.) in the day, that is, 6 grains (0.4 Gm.) at 6 A.M. to enable him to dress at 8 A.M.; 6 more at 10 A.M., 2, 6, and 9 P.M., together with  $\frac{1}{25}$  grain (0.0027 Gm.) of trinitrin at 10.30 P.M. to enable him to ascend the stair and get to bed. This kept him in perfect health, barring the seizures, which were always at hand if a tabloid chanced to be omitted. No physiological effects whatever were at any time manifested. Walsham used it with good results in **aortic regurgitation** accompanied with cardiac pain, and also in **Raynaud's disease**. S.

**ESOPHAGUS, DISEASES OF.**  
—**MALFORMATIONS.**—*Congenital occlusion*, due to the fact that during embryological development the invagination forming the mouth fails to open into the posterior end of the primitive intestine; *diverticula*, of similar origin, and *fistula*, due to incomplete closure of the branchial clefts, represent the main malformations met with in this region. *Congenital narrowing*, due to abnormal thickness of the wall or to the presence of membrane or web, and *congenital dilatation*, are also, though very rarely, witnessed.

Case in which the patient had had trouble with swallowing for fifteen years. The examination disclosed, about an inch below the cricoid cartilage, a thin web which surrounded the esophagus. It was in the form of a diaphragm with a small central opening. The nature of the web did not become clear until the writer put the mechanical dilator through the aperture, spread the dilator and pulled it back a little. The manipulation put the whole diaphragm on the stretch and made its real character plain. The ring of tissue was then divulsed by pulling the dilator up. After this soft bougies were passed at intervals three times. The patient was quickly and easily cured. Mosher (*Laryngoscope*, Nov., 1911).

Three unusual cases of congenital stenosis of the esophagus. The symptomatology of the cases was very similar and consisted in the following: When fed, the baby choked and the mouth and throat seemed full of mucus. The child sucked and swallowed well, but after a few minutes strangled and the feeding came up again. The stool consisted entirely of meconium. A catheter passed into the esophagus was arrested about 10 cm. from the gums and could be passed no farther. The children lost weight rapidly and died. An autopsy obtained in one of the cases showed the lumen of the esophagus to end sharply about one-third of the distance from the epiglottis. From here downward a narrow band replaced the esophagus to just above the cardia, where it reappeared. In 4 other cases, in children who were respectively 11, 6, 3, and 5½ years of age, there was only partial obstruction of the esophagus. The first 2 were due to congenital narrowing, the third to cardiospasm, the fourth to hysteria. All vomited solid food immediately after swallowing, and had been fed from birth on liquids. X-ray plates of the first 2 showed the lesions, while the plates of the last cases showed no evidence of narrowing. J. L. Morse (*Archives of Pediatrics*, July, 1912).

In a case observed by the writer, the esophagus ended abruptly with a slight dilatation just above the level of the bifurcation of the trachea, having no connection with the latter at that point. At the same level, in the middle line posteriorly, a narrow tube, with a lumen of about 1 mm., opened from the trachea and gradually widened until it joined the cardiac end of the stomach. Theron (*Brit. Med. Jour.*, Apr. 10, 1926).

**PEPTIC PERFORATING ULCER.**—This class of ulcer is rarely met with in the esophagus, but its recognition is very important owing to its serious nature.

**Symptoms.**—The most typical and constant symptoms of the condition are: Pain, which is severe and comes on immediately after food, the site of the pain being at the lower end of the sternum and a little to the left of it. Pain is also felt between the shoulders. Vomiting is the next most constant symptom. Dysphagia is present in more than half the cases. It is due to reflex spasm of the muscle of the esophagus from pain, and it is the main diagnostic point differentiating the condition from gastric ulcer. Hematemesis is also a very common symptom. (Miller.) The esophagoscope, carefully employed, will be helpful in identifying this condition.

**Etiology and Pathology.**—Regurgitated gastric juice or islands of gastric mucosa aberrant in the mucosa seem to underly this condition. The ulcer is usually single. It may extend into the stomach, and independent ulcers may occur in the stomach or duodenum. The situation is usually close to the cardiac orifice, and the right posterolateral wall appears to be the commonest site. The condition is usually found in middle life. As regards sex, of 45 cases in which the

sex was specified, 31 were males and 14 females. This preponderance of the ulcerations in the male corresponds to what one knows of duodenal ulcer.

Personal case and 14 on record in which the peptic ulcer was confirmed by autopsy. None of the cases had been correctly diagnosed. This is not surprising, as in only 5 cases were there any symptoms in the esophagus, pain or difficulty in swallowing, and in 3 of these gastric disturbances predominated. Regurgitation of the gastric juice into the esophagus was favored by stenosis at the pylorus or duodenum or by hour-glass stomach in 7 cases, and in most of them the cardia was much enlarged. In 8 of the 15 cases there were coexistent gastric or duodenal ulcers. **Dietetic measures** should be instituted on suspicion of peptic ulcer in the esophagus, or direct **endoscopic local treatment**. The most effectual measure, however, is prompt **gastrostomy** which rests the esophagus and gives it a chance to heal, thus warding off impending hemorrhage or perforation. Kappis (Mitteil. a. d. Grenzgebieten der Med. u. Chir., xxi, Nu. 5, 1910).

Two cases of peptic ulcer of the esophagus. The ulcer in the first case perforated into the left pleura; in the second case no perforation occurred. In the first case a diagnosis of perforated gastric ulcer was made, and in the second a diagnosis of gastric ulcer. In both cases acute abdominal symptoms occurred; laparotomy was performed, and nothing abnormal was discovered. Both cases ended fatally. C. G. Watson (Brit. Med. Jour., Nov. 2, 1912).

**Treatment.**—As peptic ulcer of the esophagus is generally secondary to some lesion elsewhere, the latter demands attention. The ulcer itself requires the same treatment as gastric ulcer, as to drugs. **Bismuth** insufflated through an esophageal tube may serve also as an excipient for

**morphine** or **cocaine** to counteract the pain, which is usually severe. Applied a few minutes before meals, such a combination facilitates greatly the ingestion of food, thus antagonizing the tendency to emaciation. Silver nitrate should be avoided in these cases, as it tends to encourage the formation of cicatricial bands and therefore to produce stenosis. After the ulcer has healed careful **dilatation by means of esophageal bougies** is necessary. In some cases, **surgical measures** become needful.

Case of ulcer in the esophagus, 2 cm. above the cardia, which first revealed its presence by symptoms of perforation and acute peritonitis. As it proved impossible to suture the perforation and the patient was almost moribund, the writer drew up the gastric fundus and wrapped it around the lower end of the esophagus, holding it in place by a few sutures 5 or 6 mm. beyond the perforation. The peritoneum was filled with a grayish, odorless fluid, but he drained it away and introduced besides into the peritoneum a large tube through a buttonhole in the iliac fossa on each side. The operation was completed in fifteen minutes and as soon as the patient had been returned to bed, half sitting up, the writer connected one of the iliac fossa tubes with a tank of **oxygen**, thus flushing out the peritoneum with a continuous stream of oxygen, supplemented by **proctoclysis**, flushing the rectum with a continuous stream of hot **saline solution** through a two-way tube, and the ordinary stimulants. The patient was a woman of 25 and her condition was very precarious for twenty-four hours, but then she rapidly improved and the oxygen was discontinued the sixth day. The eleventh day the temperature rose a little and very little pus escaped through the drains; so he connected one tube with the oxygen tank again, and pus poured anew out of the drains. The oxygen

was discontinued the fourth day and the patient left the hospital in good condition the thirtieth day after the operation. The author makes a point of connecting each of the drain-tubes in turn with the oxygen tank, extolling this continuous flushing with oxygen as a most important aid in **drainage**. Of the writer's 12 patients with diffuse septic peritonitis treated with **oxygen** he was able to save 6, and still another recovered from the diffuse peritonitis, but succumbed later to an unsuspected complication. His proportion of recoveries has thus increased from 29 to considerably over 50 per cent. L. Sencert (*Archives gén. de chir.*, Nov., 1911).

As stated by the writer, both X-ray examination and esophagoscopy are essential and mutually supplementary in diseases of the esophagus. The former should be done first, the fluoroscope also being employed, as it may prove sufficient. Barjon (*Lyon méd.*, Mar. 10, 1922).

### **PRESSURE DIVERTICULA (PHARYNGOCELES).**

**Symptoms.**—A pressure diverticulum may occur as the result of inflammation or injury; the esophageal wall is weakened, a portion of it bulges out, forming a circumscribed sac, or hernia, through the muscular coat. While small, a pouch thus formed is hardly noticed, but, as small particles of food find their way into it, it is gradually enlarged, projecting downward. It may become several inches deep, is usually elongated, and appears externally as a pear-shaped growth between the larynx and the sternomastoid muscle. It may, by its pressure, displace the esophagus and the larynx, causing violent coughing through pressure upon the superior laryngeal nerve, and dyspnea. The external swelling may suggest a goiter. (See cuts.) Dysphagia, fetor of the breath, regurgita-

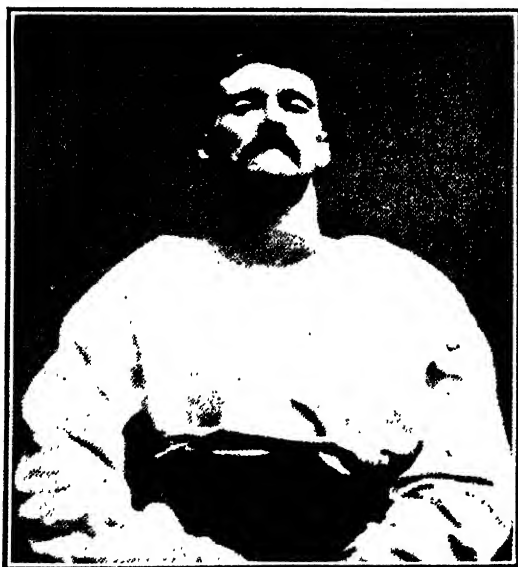
tion of ill-smelling masses of sodden food, and local pain are experienced in severe cases. Death from inanition has resulted.

**Diagnosis.**—A diverticulum may easily be recognized by palpation, especially when the patient is lying on his side, the tumor being upward. When it contains air, pressure upon it causes this to pass out and its size is reduced; when it contains food, pressure either causes marked lateral displacement of the esophagus or the food is forced up into the esophagus and mouth. It is often enlarged after meals. The sound may be used; it should be bent so as to enable it to enter the cavity, and be handled with great gentleness. (See annexed cuts.)

The examination should be conducted in a routine manner, the esophagoscope being used last, bearing in mind always the danger of a rupture of a possible aneurism. In making the examination with the X-ray, the introduction of a soft tube filled with shot (Mayer) may take the place of bismuth.

In 4 of the 6 cases reported by the writers there was an apparent oversupply of saliva, which they deem of pathognomonic significance. Advancing age may furnish a reasonable cause for most of the diverticula of the esophagus, except for those caused by a previous inflammatory condition in and about the esophagus. The pouch is most likely to occur at the upper end of the esophagus, because the direct pressure brought about by the act of swallowing seems greater in the intrapharyngeal region than elsewhere. Jewett and Lichty (*Annals of Clin. Med.*, Dec., 1925).

**Etiology.**—Inflammation and injury to the muscular coat are the predominating factors. It is usually observed in men, and at the spot



Esophageal diverticulum resembling parenchymatous goiter. (*William Robinson.*)  
(Practitioner.)

where the pharynx ends to become the esophagus. The congenital forms are usually situated near the inferior constrictor.

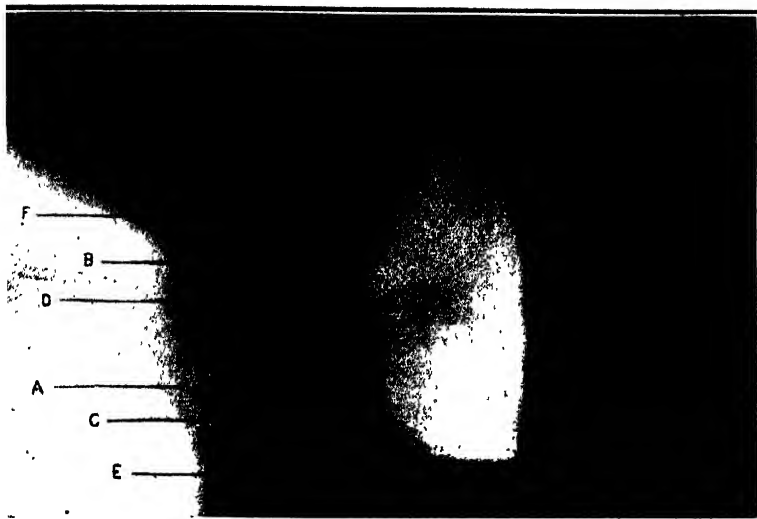
**Treatment.**—The treatment of pharyngocele is essentially surgical, if cure is to be obtained. Interference with deglutition preventing adequate nutrition, the **stomach-tube** or **rectal feeding** must be employed, as in dilatation of the esophagus. The great trouble with these cases is that decomposing food masses tend to produce inflammation in and about the sac; **lavage** of the latter is therefore of great need. It is done much as is that of the stomach, the tube being passed into the diverticulum. The application of **astringent and antiseptic solutions** to the atonic mucosa is often of benefit, as is also the regular use of **electricity** by means of the esophageal electrode. **Rest and general hygiene**, which may have to be supplemented by the administration of **sedatives** and **plentiful nourishment**, should be insisted on. Fat is an especially important article of **diet**, and may conveniently be given in the form of melted butter or olive oil a short time before meals. The following are some of the foods which may be included in the dietary: Beef-juice, rich soups and broths, including those containing cream, eggs; purée of all vegetables which do not have tough fiber, among them being purée of spinach, beans, peas, celery, asparagus, and potatoes; milk and cream; cocoa, chocolate, coffee, and tea; eggs, raw or soft; scraped meat and fish chowder; porridge made from thoroughly cooked breakfast cereals; a few sweets, such as bees' honey; calf's-foot jelly, and various simple custards.

Where the diverticulum has not occasioned any symptoms beyond that of mild distress, we may content ourselves with occasional **washing out** of the diverticulum and care as to diet. Where, however, emaciation exists, the diagnosis having been firmly established, radical operation may be performed with success. Whether a previous **gastrostomy** should be done or not must be decided for the individual case, but enough information is at hand to show that the operation for pharyngo-esophageal diverticulum is readily performed and reasonably safe. Stetten has collected statistics of 60 radically operated cases; of these, 50 patients were cured and 10 died, a mortality of only 16.6 per cent. Mayer (Med. Record, July 2, 1910).

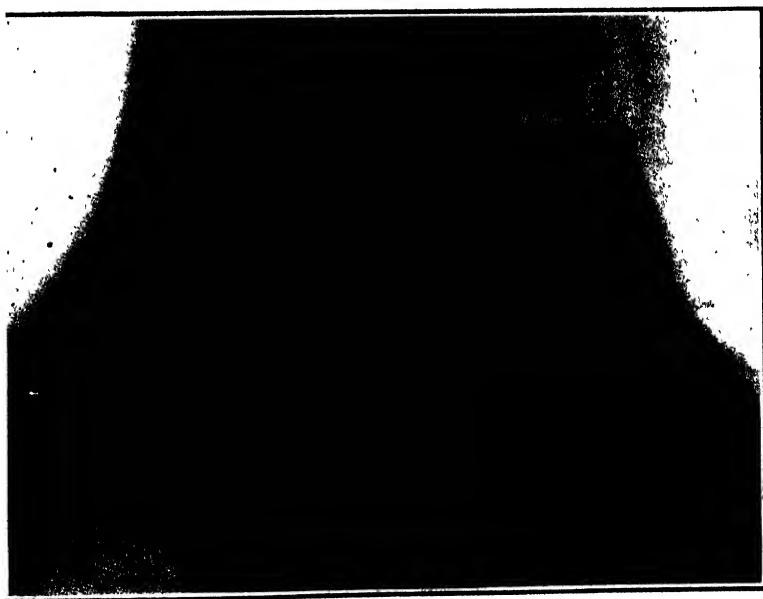
*Webs of the esophagus* may follow trauma or any disease which causes ulceration, and they may be of varying size and cause symptoms in proportion to their size. They are situated behind the cricoid cartilage, and neither the fluoroscope nor the X-ray may be able to detect them. Webs are best treated by **cutting**, aided, if necessary, by **divulsion** with the aid of the esophagoscope. The author's 3 cases of cutting the common wall have shown that this procedure is easy of accomplishment, is probably safe, and results in a clinical cure. The best method of making a diagnosis is to give general anesthesia and to use the bougie and ballooning esophagoscope. Mosher (Surg., Gynec. and Obstet., Aug., 1917).

### TRACTION DIVERTICULA.

This is a form of diverticulum which presents itself near the bifurcation of the trachea, in the anterior wall of the esophageal canal. It is generally associated with inflammation of the lymph-glands in this locality. Local inflammation followed by ulceration gives rise to cicatrices which by their contraction draw on the esophagus, *i.e.*, exercise



Side view. *A*, larynx; *B*, pharynx; *C*, mouth of diverticulum; *D*, air in upper part of sac; *E*, upper level of bismuth pap in sac; *F*, hyoid bone.



Front view.

X-ray picture of large diverticulum. (*William Robinson.*)  
(Practitioner.)

traction upon it, forming a cavity opening into the esophageal canal by a funnel-shaped orifice.

**Symptoms.**—Mechanical irritation is occasionally produced by the retention of food, and ulceration may follow, attended by its usual complication—perforation. A fistula between the esophagus and the bronchial tract may be followed sooner or later by pneumonia.

The pleura and pericardium may also be reached. In the majority of cases the symptoms are slight; it is only on account of the possible mortal complications that traction diverticula demand attention. The X-ray and esophagoscope are as useful here for diagnostic purposes as in the form previously described.

**Treatment.**—Surgical removal alone affords protection against possible complications.

### FOREIGN BODIES IN THE ESOPHAGUS.

Foreign bodies frequently become impacted in the esophagus, fish-bones, pieces of meat, pins, tacks, artificial teeth, coins, and buttons representing the class of articles found in the majority of cases.

**Symptoms.**—These vary according to the shape, size, and location of the impacted agent. A large mass, such as a piece of meat, may become engaged behind the larynx and hold the tip of the epiglottis down, completely closing the laryngeal cavity. Here, intense dyspnea soon comes on and death from asphyxia may promptly follow.

Again, a part of a bolus may invade the larynx and cause violent spasm; asphyxia here becomes possible from two causes: spasm and

reduction or total closure of the respiratory area.

Small bodies in the esophagus may produce the same symptoms, but, as is the case with large masses,—meat, bread, etc.—they seldom give rise to dangerous symptoms, unless the larynx is involved by pressure, puncture, or the epiglottis is held down in some way.

A new diagnostic sign of esophageal foreign body was contributed by the writer. Moving the trachea or the larynx toward the point of localized tenderness, as indicated by the patient, by pressure from the opposite side of the neck, causes a marked increase in tenderness and pain at this point while the foreign body is present. If the foreign body has passed on or has been removed, there will be little or no change in tenderness by pressure from the opposite side. This sign of a foreign body in the cervical esophagus, the place of lodgment of the great majority of esophageal foreign bodies, proved positive in a large number of cases during a period of 5 years at the Bronchoscopic Clinic of the University of Pennsylvania. G. Tucker (Jour. Amer. Med. Assoc., Feb. 14, 1925).

Sharp or irregular bodies,—such as chicken-bones, tacks, etc.,—when impacted only in the esophagus,—usually at its upper portion and immediately behind the cricoid cartilage,—only cause marked discomfort and severe pain, especially marked during deglutition; but these foreign bodies are attended with little or no immediate danger.

The pain may radiate in various directions.

Hemorrhage, or rather, slight bleeding, is occasionally produced.

After some time, varying with the size and shape of the body, the acute suffering ceases and pain is only experienced during deglutition.



If the impacted body is low down, which is frequently the case when it is small, it is only at this time that its true location can sometimes be established, the sensations before this being misleading. But the pain even at this time may only indicate the location of a lesion produced by a rough or sharp body during its passage to the stomach. Bronchoscopy and esophagoscopy are so important in this condition that they should always be employed when the location of the foreign body is at all in doubt or where it cannot readily be reached. The fluoroscope screen has also been used with profit.

It is remarkable that more general use is not made of bronchoscopy and esophagoscopy, while too much reliance is placed on roentgenoscopy, percussion and auscultation, and too little credence given the patient's statements. In three personal cases, the presence of the foreign body had been denied by previous examiners while direct visual inspection revealed it at once. One patient was an elderly man who applied for a "remedy for his cough;" only by persistent questioning was it finally learned that his cough had come on after he had "swallowed something the wrong way" some time before. Although there were no objective findings, yet the bronchoscope showed three slivers of bone which were readily removed. *Reinking* (*Deut. med. Woch.*, Nov. 30, 1911).

In all cases in which a foreign body is either swallowed or inspired, a radiograph should be made by a competent person before any attempt is made at its removal. This is especially important in cases of sharp bodies. If the foreign body is dense enough to be revealed on a plate, the diagnosis by this means is easy; but even in those cases in which a vegetable foreign substance is not opaque to the Roentgen-ray, a great deal of

information can still be obtained. A grain of corn, for instance, lodged in the bronchus will not cast a shadow on a photographic plate, but its presence can usually be determined by the slight changes in the lung itself, caused by a localized pneumonia, or by a blocking up of certain air-cells. The same is true of vegetable foreign bodies in the esophagus; for while the body itself cannot be seen, information especially as to its location can be obtained by giving the patient bismuth, either in the form of a capsule or in gruel, and watching the passage of the preparation down the esophagus with the fluoroscope. If a foreign body is present, the bismuth will be stopped or at least hesitate at the obstruction. *Bowen* (*Ohio State Med. Jour.*, July, 1911).

Left *in situ*, foreign bodies always tend to create local lesions, unless, as sometimes happens, spontaneous expulsion occurs after the primary local irritation and the general excitement of the patient has ceased. Local inflammation is caused, the tissues become softened; abscesses arise which may burrow in various directions, sometimes reaching into the pleura, the pericardium, the mediastinum, or the larger vessels, including even the aorta. The foreign body itself may follow either of the channels formed and cause death by reaching any of the organs of the thoracic cavity. Needles particularly are prone to migrate in various directions and sometimes appear at a spot quite remote from the gullet and totally disconnected with it as to continuity of tissue.

A few patients having died from foreign bodies in the esophagus in the writer's service, some lessons have been derived therefrom. Among them is the necessity for examining the opposite side of the esophagus when the foreign body is removed

from without. When it is large and has been impacted for some time the tissues are likely to be injured all around, and especially at both ends of the foreign body, so that the perforation may be double and infection may occur from the side opposite the incision. It is sometimes wise to open into the esophagus from the opposite side to explore the other side; the writer found this of great advantage in one case which certainly would have terminated fatally without it. The first point to be ascertained is the nature of the foreign body that has been swallowed, whether it has smooth or sharp edges. In one case the family related that the child had swallowed a cloth-covered button from her father's underdrawers, and as there was not much disturbance, and the child was able to swallow fluid food and did not seem much incommoded, while the Röntgen picture showed the button lodged not far down, several days were allowed to elapse while a suitable button catcher was being made, with which the button was finally safely removed. But instead of being as described, the button was of another kind and had sharp edges which had burrowed into the walls and the child died of sepsis two days later. Another lesson learned from his experience is that the Röntgen-ray examination should be done by an expert. In 1 case the radiograph was said to show the foreign body in a bronchus, and tracheotomy and bronchoscopy followed at once, but no trace of the foreign body could be found. Another radiograph showed the foreign body in the cecum. It had evidently been in the esophagus when first seen. The foreign body is liable to induce spasmodic contractions which renders dangerous any attempt at instrumental exploration. V. Uchermann (Jour. Amer. Med. Assoc., from Norsk Mag. f. Lægevidenskaben, Dec., 1910).

There may be no history of the accident. Cough and dyspnea, if present, indicate a foreign body in the

air passages. Difficulty in swallowing points to the esophagus. A foreign body may be present in the absence of symptoms. A pin impacted in the larynx 13 years caused only occasional fits of coughing. The only symptom may be a foul breath. A large foreign body in the esophagus may mislead the surgeon to perform tracheotomy because of dyspnea and stridor due to pressure on the trachea.

The early symptoms, however, are as a rule sufficiently characteristic and localizing. In general the symptoms are: (1) obstructive, from the size of the foreign body or from spasm; (2) irritative, produced by the presence of the foreign body, or (3) inflammatory. H. Tilley (Lancet, cxciv, 283, 1918).

Small bodies that pass into the stomach seldom give rise to trouble, being usually passed *per anum* a day or two later. In one of my cases, a child 3 years of age, the foreign body was a screw one and a half inches in length. It was passed on the third day without having caused the least discomfort. Large bodies, especially if sharp and hard, may, however, give rise to highly dangerous complications.

**Treatment.**—It is important to bear in mind, in all such cases, that a scratch or erosion of the mucous membrane produced by a passing angular bone—a fishbone, a pin, etc.—gives rise to symptoms simulating the actual presence of such a body. It is quite difficult at times to convince the patient that there is nothing in his gullet.

Cases in which dyspnea is a symptom demand immediate assistance. I have found this to be afforded most promptly by passing the index and middle fingers of the right hand into the mouth (which makes it possible to reach farther down than when one

finger is introduced) and inserting the *middle* finger into the *left* pyriform sinus. The middle finger is then passed rapidly behind the larynx. The portion of the foreign body in the esophagus is thus reached and generally swept aside, drawing out of the larynx the part engaged in it or holding down the epiglottis. If it is impacted, the index finger is brought into use, and by closing upon the middle finger a grasp is obtained upon the obstructing substance. In some cases the larynx is deep-seated and is reached with difficulty, but the mouth of the patient can stand considerable stretching, if need be, considering the imminent danger of death. This procedure is, of course, only applicable in cases in which the foreign body is situated in the upper part of the esophagus and close to the larynx, but, as already stated, these alone expose the patient to immediate death.

When dyspnea is not present, the laryngeal mirror often greatly assists in the examination of the cavities involved, and it is rare, with a good light, that a body situated not far below the larynx cannot be detected. It also assists in properly introducing and directing any instrument or forceps that may be introduced. Round and smooth articles may be pushed down with a probang when they cannot be extracted with forceps. The horsehair probang, Graefe's coin-catcher, etc, are useful, but they must be used with gentleness. Emetics should never be used, since the contractions of the esophageal muscles tend to force the body through the walls of the organ.

When fishbones, meat, or meat-bones are impacted, **vinegar** hastens their disintegration and small quan-

tities may be sipped. Foreign bodies that have passed into the stomach are said to be assisted in their migration through the intestinal tract by the use of **mashed potatoes** as food, but this, of course, will depend upon the nature and shape of the foreign body ingested.

Unless a competent esophagoscopist is at hand, the **bristle bougie** is the best device for removing foreign bodies, such as pins or fishbones, from the esophagus. A foreign body, if not too large or rough, may be pushed down into the stomach. When coins or similarly shaped bodies have lodged in the esophagus, if their position can be ascertained by means of the esophageal bougie or a skiagraph, either the bent esophageal forceps or an eight- to twelve- inch hemostat may often be successfully employed in their removal, even when the esophagoscope has failed to locate the offending object. The distance from the teeth to the object is measured, the instrument passed to its vicinity, opened anteroposteriorly, pushed gently for about an inch, and closed, and in most cases it will grasp or enclose the offending body. Unless the esophagus is inflamed it is not very sensitive, and so anesthesia is unnecessary unless the patient is nervous. If thought necessary, **cocaine** from 10 to 20 per cent., in a 1:4000 to 2:4000 solution, may suffice. In children over 4 or 5 years, excitable adults, or spasm of the esophagus, ether is indicated. To pass the esophagoscope the patient should be placed on the back with his shoulders from four to six inches beyond the end of the table, the head bent backward and supported by an assistant. The mouth-gag is used and pressure on the trachea avoided. The essentials for successful passing of the esophagoscope are that at first the head be bent backward, so as to straighten the cervical curvature and bring the axis of the oral cavity parallel with that of the esophagus, but as

soon as the mouth of the esophagus has been passed the head must be brought slightly forward so that the instrument is directed downward and backward at an angle of about ten degrees. Ingalls (*Amer. Jour. of Surg.*, Jan., 1912).

Irregular large bodies, tooth-plates, large bones, etc., when inaccessibly located, demand **esophagotomy** (*vide supra*) or **gastrotomy** (see STOMACH, SURGERY OF). **Tracheotomy** is liable to give better results in the hands of the general practitioner than tedious attempts at extraction by the natural route, with the inevitable injury from them and the bleeding.

**Esophagotomy** is the modern method of treating cases of perforation of the esophagus by foreign bodies. The case reported is a sad commentary upon the frequent failure of ordinary attempts at removal in such instances. The foreign body consisted of a small piece of bone which the patient, a woman 53 years old, stated that she had been able at first to feel with the finger in the upper throat. A physician called three days afterward was said to have pushed down the bone with the stomach-tube, and in this way probably caused so much damage to the esophageal wall as to lead to a severe infection and inflammation. When admitted to the hospital she was in a marked septic condition, with a phlegmonous process in the neck and mediastinum. Operation was at once resorted to, the mediastinum being opened on both sides and an abscess about the esophagus exposed and evacuated. This was followed by esophagotomy and introduction of a tube to permit of feeding. Convalescence was rapid, the wounds healing except on the right side, where discharge of a purulent secretion persisted. On the twenty-ninth day, when the patient was no longer in the hospital, a profuse hemorrhage took place from the wound in the neck on the right side, which necessitated

ligature of the right common carotid. The woman recuperated, but nine days later developed a cerebral abscess and basal meningitis, with fatal termination. T. Jurasz (*Intern. Jour. of Surg.*, from *Med. Klinik*, Nu. 31, 1912).

An instrument having distal illumination is the best. Strict asepsis, a plentiful supply of swabs, and some form of suction apparatus for keeping the field free of mucus and blood are important in technique.

As a rule urgent dyspnea demands immediate **tracheotomy**. The bronchoscope can then be passed through this opening. If dyspnea persists after removal of the foreign body, **intubation** or in extreme cases tracheotomy may be necessary. **Esophagoscopy** is as a rule not so urgent as **bronchoscopy** but is definitely indicated in all cases of lodged foreign bodies except in cases of traumatism or inflammation of the esophagus, in some cases of aneurism or serious vascular lesion, and in cases in too critical a condition to withstand the procedure. The mortality in skilled hands is very low, but the "occasional operator" will be a source of danger to the community. H. Tilley (*Lancet*, cxciv, 283, 1918).

## INJURIES OF THE ESOPHAGUS.

The esophagus is often involved in injuries inflicted with suicidal intent, the ingestion of corrosive fluids and attempts at throat-cutting being the chief casualties of this kind met with in practice. Many accidents occur also through the accidental swallowing of acids or strong alkalis,—concentrated lye, for instance,—or a household disinfectant, such as carbolic acid, or, again, boiling tea or coffee from the spout of a vessel. A corrosive substance taken by a suicide is usually taken hastily and thrown, as it were, far back into the mouth. Spasm of the larynx usually ensues

and collapse follows. The same effect is generally, however, produced in accidental cases, and the lips, the gums, or even the front part of the tongue do not always indicate the severity of the lesions produced. If death does not immediately occur from laryngeal spasm,—i.e., asphyxia and shock,—severe pain is experienced and acute esophagitis (see below) ensues. Wounds of this region due to accidents or military weapons are extremely rare, however, but one injury of the esophagus, for instance, having been recorded during the Rebellion. The protected position of the esophagus anteriorly and posteriorly seems to account for this, the sternum and spinal column acting as shields.

### ESOPHAGITIS.

**Symptoms.**—In cases arising from injury of the esophageal tissues pain is marked, especially during deglutition, unless the traumatism be of such a nature as to completely destroy the tissues and their nervous supply, as sometimes happens when caustic acids are swallowed. Under these circumstances slight pain in the periphery of the disorganized mass is the general result. The pain usually experienced is continuous and dull, and usually follows the long axis of the sternum, extending to the back and neck. Motions of the head or shoulders sometimes aggravate it. At times it is burning, especially if the lesion is not deep-seated and when regurgitation of the acid gastric contents occurs. Spasm is frequent in such cases. A sensation suggesting the presence of a foreign body is complained of.

After a lapse of time, varying with the gravity of the injury, hematemesis may occur, owing to the contraction

of the muscular supply around the ulcerated areas that are undergoing the process of repair; but this is generally of short duration. Large quantities of mucus and mucopus are often voided.

The sequelæ of these cases are usually serious. Even after slight injuries, sometimes, cicatricial stenosis occurs that leads to esophageal stricture.

The presence of blood in the food and localized pain suggest that a foreign body may be present when no other clear indication is furnished by the history. This form often becomes phlegmonous and is usually attended by a febrile reaction. Pseudomembrane may also be vomited: indicative of the form of stenosis present. Thrush, it must be remembered, may be attended by no other symptom than impediment to the passage of food.

In some cases the local inflammatory symptoms—difficult deglutition, the mucopurulent discharge, etc.—continue for some time. Such cases are termed *chronic* esophagitis by some authors.

**Diagnosis.**—In traumatic cases the history and the symptoms render the diagnosis easy. The location of the pain usually points to the seat of the lesion; this may be verified by the passage of the esophageal sound: a dangerous procedure in severe injuries. In acute esophagitis occurring in the course of febrile diseases a condition with which it may be confounded is the irritation following repeated vomiting of acid substances. The discomfort resulting from this, however, is of short duration, while the symptoms of true esophagitis are continuous and more marked.

**Etiology.**—Almost all cases of acute esophagitis are due to mechanical and chemical irritation or destruction by caustic acids, hot liquids, and foreign bodies. Cases due to the ingestion of acids are often met in connection with attempts at suicide, while the two latter exciting factors usually come into play accidentally. Carbolic acid is most frequently used by suicides, while the accidental agents are boiling liquids, concentrated lye, and spicules of bone.

Acute inflammation also occurs as a complication of infectious fevers, typhoid fever, typhus, pneumonia, pyemia, small-pox, etc., while pseudomembranous esophagitis may be caused by extension of a disease, such as diphtheria, in which a false membrane is present. Various pharyngeal disorders complicated with abscess may also extend to and involve the esophagus in the inflammatory process. Malignant neoplasms, especially carcinoma, of the esophagus may be accompanied by acute esophagitis. Among the rare causes are: the prolonged administration of tartar emetic (Laennec), vertebral abscess, laryngeal perichondritis, and hysteria.

It is occasionally met with in sucklings without explainable cause.

**Pathology.**—Desquamation of the epithelium and erosions are present when comparatively mild caustics or strong solutions of them have been swallowed, but, when such agents as pure carbolic acid, concentrated lye, etc., have been taken, the entire mucous lining may be deprived of its epithelium. It then becomes greatly swelled, and purulent infiltration usually follows the primary serous infiltration. The mucous layer may

thus be detached from the underlying tissues. Foreign bodies may also cause deep-seated lesions and be surrounded by a cushion-like mass, causing temporary esophageal stenosis. Gangrene occasionally follows, necrotic masses being ejected, generally with vomitus. The local disorder occurring as complication of fevers, etc., is usually less marked, though diffuse purulent inflammation occasionally occurs.

**Treatment.**—The treatment must necessarily be symptomatic since the inflammation is but the expression of local repair, though we may influence this process so as to avoid stenosis as after-effect. When one is fortunate enough to discover the cause at once, local measures may prove useful. If the lesion is due to some mineral acid, **lime water** should be used; if to caustic alkalis, **vinegar** is indicated. **Iced fluids** and, if the patient can swallow, **white of egg** are particularly useful in all cases due to corrosion. An **ice-bag** around the **neck** often subdues the pain.

**Feeding**, when possible, should be limited to cold, soft, bland substances, preferably milk, soft-boiled eggs, or hard-boiled egg-yolk reduced to flour and mixed with the milk. If deglutition is difficult, the upper portion of the esophagus—which is usually the seat of severest lesion—and the pyriform sinuses (on each side of the larynx) can be slightly anesthetized with a spray of 4 per cent. solution of **cocaine**, applied with a curved-tip atomizer so as to localize it. Or, **orthoform** may be insufflated with a powder-blower in the same region; besides producing analgesia, this agent acts as an antiseptic. An injection of **morphine**, one-half hour before

meals, also reduces markedly the local hypersensitiveness during deglutition.

All these various measures are also indicated to relieve the continuous pain. Small pieces of ice allowed to melt slowly in the mouth afford comfort by causing constriction of the engorged vessels, and ice-cream is a very agreeable article of food which produces the same effect. In some cases the patient must be fed *per rectum* until disappearance of the acute phenomena.

*Chronic esophagitis* may occur as a result of the acute form, but in most instances it is due to passive engorgement of the veins owing to obstruction of the circulation through disease of some organ, the liver in cirrhosis, the kidneys in Bright's disease, etc. The engorgement may be such as to cause rupture of one of the esophageal veins and fatal hemorrhage occur therefrom. Most cases occur in alcoholics.

The writers urge the importance of Minnigerode's discovery of a light strip in the X-ray picture corresponding to air that had escaped through a perforation in the esophagus, or to gas generated in a suppurative process. They describe 4 cases, 1 with spontaneous subsidence of the disturbances after extraction of the swallowed bone. After the swallowing of a foreign body, repeated roentgenoscopy will reveal the first onset of escape of air through perforation of the esophagus wall and allow intervention in time to ward off serious trouble. Huizinga and Keijser (Nederl. Tijdsch. v. Geneesk., Sept. 19, 1925).

The treatment resolves itself into measures calculated to overcome the causative disorder. A milk or very low diet is indicated when the varicose state of the esophagus is marked,

alcohol, coffee, tea, and other agents capable of raising the blood-pressure being strictly avoided. Agents which reduce the blood-pressure are useful to deplete the engorged vessels. The following mixture, which also contains a local sedative and astringent, may be used:—

℞ *Potassii bromidi* .... ʒij (8 Gm.).  
*Tr. veratri viridis* . . ʒj (4 c.c.).  
*Bismuthi subnitrat* . . ʒiiss (10 Gm.).  
*Mucilaginis acacie* .. ʒiiss (45 c.c.).  
*Aque cinnamomi*  
 q.s. ad ..... ʒiv (120 c.c.).

M. Sig.: Shake well before using, and sip 1 tablespoonful on retiring.

During the day the effect may be kept up by means of the following:—

℞ *Acidi tannici* ..... gr. j (0.06 Gm.).  
*Cocaine hydrochlor.* . gr. ¼ (0.01 Gm.).  
*Extracti glycyrrhizæ*. gr. ij (0.13 Gm.).  
*Sucrosi* . . . . . gr. j (0.06 Gm.).

M. et ft. trochiscum no. j.

Sig.: Allow 1 to dissolve slowly in the mouth four times daily, between meals.

## STRICTURE OF THE ESOPHAGUS.

**Symptoms.**—Narrowing of the esophageal lumen—whether due to cicatricial contraction or to tumors, intramural or extramural; aneurisms, etc.—is attended by gradually increasing difficulty in swallowing, referable, in the majority of instances, to a particular spot under the sternum. At first solid food is passed with increasing difficulty, and the patient finds it necessary to masticate with great care or swallow smaller boluses. A feeling of pressure is usually experienced as the food gravitates downward, which in some cases enables the patient to gauge the steadily decreasing rapidity with which the food reaches the stomach. Later on these masses require the

assistance of fluids, and finally only the latter can pass with ease.

In 1 of 2 cases of obstruction of the esophagus witnessed by the writer, the first is of interest as showing the length of time a large, irregular-shaped, foreign body can be retained in the esophagus. The patient, a man aged 34, had swallowed his upper false teeth during sleep, temporarily causing obstruction to swallowing. For nine weeks after that he suffered no pain except during the act of swallowing, which caused him some distress. Neither he nor his physician had located the foreign body in the esophagus, but it was shown by a skiagram. The shape of the body rendered its removal by direct traction inadvisable, on account of the danger of injury to the esophagus and of possible cellulitis; it was therefore removed by an open operation at the side of the neck, which is described. Convalescence was uneventful. A. Bassler (*Jour. Amer. Med. Assoc.*, March 15, 1913).

The first effort at swallowing at a meal is generally the most arduous, the subsequent boluses passing with comparative ease. Various motions of the head are resorted to by the patient in the vain hope to assist the act of deglutition. As the difficulty increases, the patient gradually becomes weakened and emaciated through deficient nutrition.

In stricture due to cancer the contraction is rapid and death from pneumonia is not uncommon. When this does not occur, the tissues around the esophagus are gradually implicated by extension, and death occurs from marasmus due to general toxemia, this being greatly encouraged by starvation. The sense of hunger, however, is not acute. The vomited materials are often tinged with blood, and the general facies of the patient soon serves to indicate the presence

of a malignant neoplasm. Glandular infiltration occurs late in the disease.

Three cases of benign cryptogenic stricture of the esophagus which have occurred in the writer's practice within a year. All were in the cervical part of the esophagus and the patients were women. One was 32 and the others each 67 years of age. In 1 there was also a pocket which was opened. When an elderly or middle-aged patient complains of difficulty in swallowing it is usually apt to be diagnosed offhand as due to nervousness or cancer, according to the length of time it has existed. W. Lerche (*Jour. Amer. Med. Assoc.*, April 19, 1913).

Although about 60 per cent. of esophageal obstruction is due to carcinoma, the writer says the other 40 per cent. can be cured. Benign stenosis will go on to complete obstruction if allowed to remain untreated. Even a cardiospasm will cause death from prolonged lack of water and nourishment. X-ray examination should be made in every case of dysphagia. If the diagnosis is not made at the first examination, it should be repeated at intervals of 2 or 3 weeks. An invisible foreign body must be excluded as a cause of dysphagia. Osmond (*Radiology*, Oct., 1925).

**Diagnosis.**—Certain points serve to locate the seat of the stricture. Regurgitation of the food usually occurs immediately when the stricture is situated near the upper orifice. That the rejected food has not reached the stomach can easily be recognized by the absence of the characteristic odor. The material ejected is also alkaline instead of strongly acid: a valuable diagnostic feature. When the narrowing is low down the esophagus is dilated above, and the food is accumulated in the pouch-like cavity formed. Regurgitation, instead of occurring promptly after the inges-



tion of food, only takes place several hours later, and is mixed with considerable mucus. Here, again, the material ejected is not acid, having failed to reach the stomach. The accumulated food sometimes causes dyspnea by pressing upon the trachea.

The X-ray method aided by an opaque medium to afford an outline of the esophageal canal permits an early recognition of the stricture. Esophagoscopy is, of course, of great value in this connection.

Stricture of the esophagus as a result of increased mediastinal pressure is not an uncommon occurrence and is rightfully looked upon as an important sign of mediastinal disease. Such a pressure upon the esophagus may be exerted by enlarged mediastinal glands, malignant disease of the mediastinum, aortic aneurism, mediastinal or spinal abscess, pericardial effusion, chronic adhesive mediastinitis, etc. Lange (*Med. Rec.*, Jan. 16, 1909).

Esophagoscopy is comparatively easy in children, as the mouth of the esophagus is not closed, as in adults, but gapes rhythmically with inspiration. In cicatricial stenosis the writer introduces a narrow **bougie** with the aid of the esophagoscope and leaves this bougie in place for a few hours. This prepares the way for sounds of a larger caliber, and it is thus possible to stretch the lumen to normal size in time in most cases. If not, circular **electrolysis** through the esophagoscope renders invaluable service. He has had 54 patients with cicatricial stenosis resisting all ordinary measures. Only 10 required **gastrotomy**; all the others were cured by the above measures through the natural passages; 21 of the patients were children and all but 2 were cured. Guisez (*Bull. de la Soc. de pédiatrie*, June, 1911).

The writer calls attention to an inflammatory stenosis of the esophagus, occurring chiefly in men over 50 years

old. The difficulty in swallowing is intermittent at first; after a few years it becomes permanent, and gradually even liquids do not pass through the esophagus. The disease at this stage may be mistaken for cancer. Incompletely chewed food seems to induce spasm of the esophagus, followed by stagnation of the food and inflammation of the organ. This entails hypertrophy or sclerotic degeneration of the mucosa, with consecutive stenosis. The disease may become complicated by cancer. X-ray examination and esophagoscopy indicate the location of the stenosis. The treatment consists in repeated insertion of a filiform bougie, left for a few hours, continuing with **bougies** of a **progressively larger size**. Guisez (*Bull. de l'Acad. de méd.*, Dec. 22, 1925).

Auscultation of the esophagus may sometimes be employed with advantage; provided, however, the examination be conducted in a very quiet room. The stethoscope is usually employed, but direct application of the ear along the left of the spine—while the patient brings his shoulders as close together anteriorly as possible—is far more satisfactory. A peculiar, irregular, wave-like bruit is heard when liquid is swallowed, followed by a second splashing sound as the fluid reaches the stomach. When a stricture is present the wave-bruit and the splashing sound are varied in proportion, the latter being absent in some cases of advanced constriction or replaced by repeated splashes following one another more or less in rapid succession.

Far more precise, however, is the information acquired by means of the esophageal sound—especially the graded, olive-tipped, flexible bougie. The patient being placed upon an ordinary chair, (avoiding one with a high back), the physician stands be-

hind him. He should use his left hand as guide for the instrument, by placing it on the patient's face so as to bring the index and middle fingers over and parallel with the patient's mouth. The patient's head being thrown back, the bougie (warmed and lubricated with glycerin) should first be passed between the fingers and then introduced into the mouth perpendicularly—much as a sword-swallower introduces the weapon. The olive-tip, however, should *not* penetrate the esophageal canal by passing *over* the larynx, but into the pyriform sinus on either side of the larynx. Each sinus affords a funnel-like aperture which allows the bougie to glide easily into the esophagus, without encountering the bodies of the cervical vertebra or the cricoid cartilage. The instrument should not be forced down, but allowed to drop into the cavity by reason of its own weight. The present method of introducing the instrument over the middle portion of the pharyngeal wall, and therefore over the center of the epiglottis and the posterior surface of the larynx, is defective, and accounts for the resistance usually encountered while introducing the instrument.

Frequently a spasm of the muscles causes the instrument suddenly to be arrested; but after a few seconds this ceases and arrest only occurs at the seat of the stricture. When this happens the instrument should be allowed to remain *in situ*; after a few moments it often suddenly drops lower down. In some cases it is advisable to first anesthetize the pharynx and that portion of the esophagus within reach with a 4 per cent. solution of cocaine. When permanent arrest occurs below

the larynx, the spot (gauged by length of bougie introduced) should be estimated and a slightly smaller bougie then tried. This is repeated until one is obtained that penetrates the opening—of which it affords an approximate diameter for future comparison. In some cases only narrow catgut will pass. Gum-elastic stomach-tubes may be used, but they do not afford the exact information obtained from the olive bougie. It should not be used, however, when an aneurism is known to cause the stricture.

Great care and gentleness should invariably prevail. The procedure is not devoid of danger even in the hands of an expert, softening of the tissues, especially in the low strictures, readily yielding to the pressure of the instrument. I have witnessed a case in which a pint of milk was thus introduced into the mediastinum, as shown by the autopsy.

The presence of stricture having been determined, the history almost invariably points to its original cause. The case should be *completely* examined, however; a history of syphilis with tertiary pharyngeal symptoms may be obtained, for instance, and the stricture be ascribed to cicatricial stenosis, while in reality the true cause may be an aneurism. All the etiological factors should be borne in mind and the prevailing one determined by elimination.

In stricture due to cancer the stenosis is usually situated where the left bronchus forms a ridge in the esophageal mucous membrane, but no portion of the canal can be said to be exempt. The vomited matter is often tinged with blood and the cancerous facies soon serves to establish the diagnosis. Emaciation is generally

very rapid. The possibility that a stricture may be cancerous imposes additional care in the use of the bougie, the friability of the cancerous tissues being such as to easily yield to even slight pressure. A stricture occurring after the fortieth year in a man whose history does not present strong evidence of syphilis, tuberculosis, or local injury is usually cancerous.

**Etiology.**—Stricture of the esophagus may be congenital, but it occurs, in the majority of cases, as a result of lesions produced by the ingestion of corrosive liquids.

The frequency in children in Austro-Hungary of corrosion of the esophagus from drinking lye is shocking. At the Stefanie hospital at Budapest there have been in the last nine years 516 cases of acute disturbances from this cause, and 267 cases of cicatricial stenosis of the esophagus, all the result of leaving a solution of lye, ready to be used in washing, within reach of young children.

The writer has found it possible to examine the condition with the Roentgen rays by having the children swallow a soft porridge containing 30 or 40 per cent. of oxide of zirconium. This substance is insoluble in acids, strong alkalies, etc., and seems to have no action when injected subcutaneously into animals, so that no toxic action need be feared from it; for Roentgen work it has several advantages over bismuth. As the child swallows each mouthful of the porridge, the progress of the mouthful down the gullet can be watched with the Roentgen rays, and the regions where it passes along smoothly and where it seems to be arrested or makes its way slowly are marked and compared. By this means it has proved possible to detect multiple strictures. Flesch and Peteri (*Jahrbuch f. Kinderheilkunde*, June, 1911).

Ulceration occurring as complication of infectious diseases, particularly typhoid fever. Syphilitic ulceration of the esophagus, though, is usually followed by stricture varying in degree with the location of the ulceration and the area involved. Impacted foreign bodies, masses of thrush-fungus, local tuberculosis, injuries—*i.e.*, all conditions capable of causing severe acute esophagitis—may act as primary causes. A greatly enlarged thyroid, an aneurism, an intramural abscess, enlarged lymphatic glands, growths of the mediastinum, etc., may also, by pressure upon the esophagus, reduce its lumen. Cancer of the esophagus may act as cause.

A comparatively frequent cause of stricture is squamous epithelioma: almost the only form of neoplasm encountered in the esophagus. It is usually met with in men, and after the fortieth year.

**Pathology.**—The pathology of stricture varies with the cause, but in practically all cases due to local lesions, excepting cancer, the prevailing feature is the presence of cicatricial tissue. In cases originating from the ingestion of corrosive fluids the stricture is usually high, spasm of the esophagus generally preventing gravitation of the liquid to the lower part of the organ. In all others, even syphilis, the chances are that the stricture—there is generally but one—will not be far from the lower third, or lower down. The extent of tissue involved varies frequently, and occasionally the whole lumen of the esophagus is more or less involved and distorted. In the majority of cases in which the stricture is low, there is sacculation or dilatation of the portion above the stenosis.

**Prognosis.**—In case of cicatricial stenosis the prognosis is quite favorable under appropriate treatment. Without treatment the contraction usually reduces the lumen sufficiently to prevent alimentation, and the patient dies of slow starvation. Cases due to cancer are naturally hopeless, while the prognosis of cases resulting from pressure of surrounding growths, aneurisms, etc., depends upon the degree of curability of the latter.

**Treatment.**—The aim of the treatment is obviously to restore the lumen of the esophagus to its normal dimensions as nearly as possible, but in cancerous stricture this is hardly indicated, the neoplasm itself involving complications that bring on a fatal issue. For this reason a distinct line should be drawn between cases of stricture due to cicatricial lesions—*i.e.*, injuries, syphilis, tuberculosis, etc.—and those due to a malignant neoplasm. In all of the former **dilatation with the bougie** may be said to be required as soon as a stricture has been recognized; in cancerous stricture the procedure should not be resorted to. It but inflicts severe suffering upon the patient and involves additional risk.

The writer commends the regular passage of **bougies** as affording much comfort to the patient and enabling him to take a much larger variety of food with ease. Where the stenosis is increased by spasm, much help is obtained by the use of the **bromides** in addition. **Thiosinamine** was used with success in some cases of cicatricial stenosis in conjunction with the bougies, being given hypodermically twice a week for some weeks in each case. Walker Downie (Glasgow Med. Jour., June, 1912).

In 14 cases of practically impassable cicatricial stenosis of the esophagus, the writer resorted to **retro-**

**grade catheterization.** An opening is made into the stomach and then 10 or 15 days later, a fine catheter is passed up into the esophagus from below, under direct visual control through the gastrostomy. This allows a thread to be drawn through the esophagus, and a fine rubber tube, tied to this thread, can also be passed. The thread tied to the tube is left till the next day, when the progressive dilatation is continued. Sencert (Bull. de l'Acad. de méd., Paris, March 12, 1918).

In 1920 the writer introduced a preventive treatment of esophageal strictures caused by ingestion of lye. Out of the 226 cases treated to date, 214 were cured, 3 died on the first day, 4 died from pneumonia, 5 from perforation. He **washes the stomach** with water and gives a **fluid diet**. Introduction of the **stomach tube** begins from the second day but not until the fourth day if there is fever. The soft stomach tube is filled with fine shot. At first it is left for only a few minutes. After 6 days it may be left for half an hour. Even 4 year old children learn to introduce the tube themselves. The patient is given soft food in the second week and ordinary food in the third. Deglutition is painless in a few days. He compares the fine results of this early treatment with the inevitable strictures under expectant treatment. Salzer (Wiener klin. Woch., Mar. 12, 1925).

Cicatricial stricture may be expected in all serious injuries of the esophagus. Hence, after an accident or a local disorder known to be followed by cicatrization, stenosis should be prevented by dilatation with bougies employed in the manner indicated under **DIAGNOSIS**. **Dilatation** should be begun as soon as there is a reasonable evidence that an ulcerative process no longer exists, and be repeated daily, beginning with a medium-sized tube and ending with one representing the normal diameter

of the esophagus. The surgeon should not wait until symptoms of stenosis appear, since this often occurs only after considerable narrowing of the lumen. In some cases stenosis returns as soon as the bougies are not introduced, and the patient is required to personally use the instrument during the rest of his life. Whether begun early in the history of the case or late, the procedure is generally effective, but in old cases the tissues yield with difficulty and sometimes greatly tax the patience of surgeon and patient. It is sometimes necessary to begin with catgut, which can be left *in situ* until the following visit, when the smallest bougie can often be introduced. The catgut does not prevent the passage of liquids and the patient can be fed as usual. As large a bougie as the stricture will admit is then introduced every day, and a larger one substituted every few days until the largest number is easily passed and retained several hours daily.

In simple cases dilatation with **bougies** is used, preferably slow, from a few hours up to twenty-four hours. Complex cases require visual search to find the lumen (endoscope), which is usually lateral. **Dilatation** is instituted. Brünings has devised special probes for this internal **esophagotomy**, either with the esophagotome, a Guisez guide, or with hidden blade. Sargnon (Arch. intern. de laryn., d'otol. et de rhin., Sept. and Oct., 1912).

Dilation of fibrous strictures can be greatly hastened by the use of **electrically heated bougies**. A bougie fitting the stricture tightly is warmed to 40° C. and kept in the stricture at that temperature for 30 minutes. After its removal, the tissues being hyperemic, edematous and softened, the dilatation is resumed at once with unheated flexible bougies. Dean (An-

nals of Otol., Rhinol. and Laryn., Dec., 1921).

**Permanent tubage** of the esophagus, introduced by Symonds, of London, has won much favor. The tubes are "from 4 to 6 inches in length and are made of gum-elastic upon a silk web, the outside and inside being as smooth as possible. The upper end is funnel-shaped so as to rest upon the face of the stricture, and slightly flattened on one side (that it may not press unduly against the back of the cricoid), and the margin is perforated in two places for the attachment of a silk thread. The other end is hollow, with a lateral opening. The tube can be introduced upon a bougie, but it is more easily managed with a proper whalebone guide set in a suitable handle. The exact site of the stricture is ascertained first and marked upon the guide; the greatest gentleness must be used, and as soon as the point enters the narrowest part the tube is slowly pushed onward until the resistance to the funnel is felt; the guide is then withdrawn and the silk thread attached to the tube tied around the ear or fastened with strapping. A tube of this kind can be left for two or three months without being changed, the patient swallowing liquid food through it. As a rule, however, it is necessary to remove the tube after three or four days, as the stricture always dilates to some extent, and sometimes this must be repeated. Even if it should slip through, it will pass *per anum* or remain lodged in the stomach without inconvenience" (Mansell-Moullin). This method is said to be devoid of risk to life, and a sufficient amount of food can readily be ingested.

When these short tubes cannot be

used or when they cause cough during deglutition Krishaber's or Morell Mackenzie's long tubes, or, better still, a long, catheter-like rubber tube can be employed and left *in situ* several days at a time.

A procedure for passing very tight strictures of the esophagus, described by the writer, consists in the use of a slender (4 mm.) **steel wire** with a tiny **olive tip** or bead. The wire is pushed through a metallic tube slightly broader than the tip. The tube is curved to conform to the pharynx and introduced with the left hand like a bougie. The tip is worked through the stricture with the right hand, the tube being made to follow it as soon as it has advanced any distance. Whenever the tip is in the tube its rubbing against the latter gives notice of the fact to the operator. Dilatation of the stricture is effected by withdrawing the tube, gradually slipping larger-sized olives on the wire and pushing them through the stricture with the aid of the tube. Seiffert (Monats. f. Ohrenheilk., Nov., 1921).

Operative procedures are sometimes resorted to.

**Internal esophagotomy**, an operation based on that of urethrotomy, wherein the cicatricial bands are cut, has not given the satisfactory results claimed for it. It is only warranted in cases of annular stricture. **Esophagostomy** is preferred when the stricture is high enough to be reached through the side of the neck, the incision being made between the pharynx and larynx on the left side, toward which the esophagus leans in this region. The trachea then finds itself on one side of the incision and the carotid sheath on the other. The location of the stenosis having been determined, it is as nearly as possible made to correspond with the upper part of the incision, which should also

include the esophagus. Sometimes the omohyoid must also be incised. A rubber tube is then introduced, and the permanent fistula formed serves for its easy introduction and withdrawal. The patient can thus be easily fed, the tube passing under the stenosis. The operation is not an easy one, owing to the proximity of large vessels and other easily wounded structures.

In cancerous stricture it is inadvisable to pass **bougies**, as already stated; but a soft-rubber **catheter** with large fenestra, passed every other day or oftener, often serves to keep the passage open. It may also be left *in situ* and serve for the introduction of liquid food. **Rectal feeding** should be resorted to when esophageal alimentation becomes impossible, but when rectal feeding in turn becomes insufficient—which often happens when continued several weeks—**gastrostomy** should be resorted to. Through the opening thus obtained to the interior of the stomach it is possible to very satisfactorily supply the patient with all the food he requires. The improvement is usually rapid, and comparative comfort is insured until the toxic effects of the neoplasm bring on death.

The history of the case and examination with simple instruments soon clears up the diagnosis, but little can be done in treatment. A **gastrostomy** affords but temporary relief, although this spares the cancer the irritation from passage of food and thus has a marked palliative influence in addition to its permitting feeding. But the general toxic action of the malignant disease is not checked and it is seldom possible to keep the patient alive for more than two or three years. The retention cannula suspended in the stricture has not

given good results; gangrene from pressure may occur, and the growth of the tumor pushes the tube up out of the stricture. The same objections apply to Senator's and Schreiber's dilators. Better results were obtained with the cautious use of ordinary sounds. Local application of radium has not given good results. When emaciation begins systematically the writer advises an operation rather than to let the patient drift away with nothing done, and thus gives him a longer lease of life. Ewald (Med. Klinik, Dec. 15, 1912).

The writer reported 4 cases in which the entire esophagus was reconstructed, with excellent functional results. In a fifth case of lye stenosis the patient succumbed to pleural empyema after mere esophagostomy. The patients were all young adults, and the new subcutaneous esophagus was made from a 40 cm. segment of the jejunum. He enclosed it in a skin tube extending above and below the suture points. The whole procedure took about 1½ years. J. Jankovskis (Jour. de Chir., June, 1925).

## DILATATION OF THE ESOPHAGUS.

**Etiology and Symptoms.**—Dilatation of the esophagus may be congenital, as stated, but in the majority of cases it occurs as the result of stenosis of the lower end of the tube, which, by its resistance to the passage of food, causes its accumulation in the esophageal canal. To compensate for this the walls become greatly hypertrophied. This condition is followed, as elsewhere, by softening, which in turn causes the canal to yield to the pressure of its contents, and to become greatly enlarged.

Remarkable esophageal dilatation observed. It was fusiform in shape, the smaller portion of which extended as high up in the neck as the cricoid cartilage. The esophageal sac held as much as 1750 c.c. of water. Fried-

enwald, Cotton and Harrison (So. Med. Jour., Sept., 1917).

Generally, small quantities of food are passed into the stomach at a time, and the pouch-like cavity becomes gradually emptied between meals. But regurgitation occurs when this process is too slowly performed, and the frequent invasion of the larynx by the food thus brought up causes strangling and cough, besides the dysphagia which the patient simultaneously experiences.

Cases of esophageal dilatation are frequently but erroneously referred to as examples of cardiospasm. Histologically there is found no hypertrophy of the muscles of the cardia such as might be expected if spasm had occurred. The diagnosis is made with a bismuth meal. Shaw and Woo (Lancet, Dec. 2, 1916).

Meltzer's swallowing sound is helpful, when detected, in identifying the case as one of dilatation.

Both cardiospasm and idiopathic dilatation of the esophagus are present if Meltzer's swallowing sound is clearly heard either immediately or seven seconds after deglutition. Cardiospasm is frequently present if it is considerably delayed from 12 to 20 seconds after swallowing water, or if it is now delayed and now absent. Einhorn (Med. Record, March 1, 1913).

The bougie may be used to advantage, the large dimensions of the cavity and the narrow orifice met below being characteristic. Side-pouches may cause the sound to be arrested if it is not introduced perpendicularly or if distention of the canal is present.

Typical example of the "pulsion" diverticulum and of diffuse dilatation in the upper and lower parts of the esophagus. In the one case the father of the patient had a similar affection, confirming the congenital

tendency to special weakness of the muscle at the junction of the pharynx and esophagus. The physiological internal pressure in the esophagus, to propel the food along, causes protrusion of this part of the wall, with formation of a diverticulum in time. As it is due to the propulsion of the food, it is called a "pulsion" diverticulum. The disturbance in swallowing, regurgitation, tumor in the neck and murmur suggested the diagnosis, which was confirmed by Roentgen-ray examination. F. Umber (*Arch. für Verdauungskrankheiten*, Feb., 1910).

**Treatment** is futile unless any stricture present be itself reduced, either by the sound or by surgical removal of the constricted area.

When strictures can be completely eradicated, the esophagus tends to resume its normal caliber, but this is aided by galvanism, the positive pole being passed into the esophagus and the negative applied externally, preferably between the shoulder-blades.

A dilated esophagus allows remnants of food, layers of mucus, etc., to attach themselves to its walls and to accumulate in the fundus of the pouch formed. The latter should be washed out daily with warm water through a stomach-tube. If the lower stricture is narrow, much of the fluid containing the offending substances is returned. After each meal the patient should perform exercises consisting in compression of the chest after deep inspirations to force food into the stomach.

The cardinal feature from the start is to nourish the patient. Fluids, milk, cream, soft-boiled eggs, and other semifluid foods can be ingested, and if taken in small quantities and at intervals, pass, though slowly, until the stricture is too narrow even for small sounds. Swallowed with the

usual speed, even such food accumulates, and is regurgitated, causing sometimes dangerous strangling. If food no longer passes alone, a Symonds tube can be used, or rectal feeding resorted to, pending surgical removal of the strictures.

Insufflations of finely powdered tannin and bismuth, equal parts, are sometimes helpful after washing out the esophagus, to promote contraction.

Analysis of 91 cases of diffuse dilatation of the esophagus treated by dilating the cardia with the hydrostatic dilator, no anatomical stenosis having been detected. Four of the patients died after treatment, the known causes being pneumonia, tuberculosis, and rupture of the esophagus, with the cause unknown in 1 case; 73 were completely relieved from their dysphagia and 11 were not. The cures have lasted from 1 to 7 years. H. S. Plummer (*Jour. Amer. Med. Assoc.*, June 29, 1912).

Case in which 8 cm. of esophagus could be pulled down into the abdomen. The esophagus was fastened to the diaphragm with 3 sutures, and a longitudinal incision 4 cm. long made in it in the cardial region and sutured transversely. A cure resulted, fluoroscopy later showing the esophagus as a straight channel to the stomach. Sencert and Simon (*Rev. de chir.*, lix, 355, 1921).

Idiopathic dilatation of the esophagus was observed by the writer 4 times in less than a year. In one a sarcoma had developed secondarily. Great benefit was realized in one case by dilating exercises with 2 bougies at a time. The woman was taught to continue these herself, and there is no dysphagia or other symptom. Cascao de Ancaes (*Lisboa Médica*, Sept., 1925).

**CARCINOMA OF THE ESOPHAGUS.**—This form of tumor is relatively rare in the esophagus, Walshe,



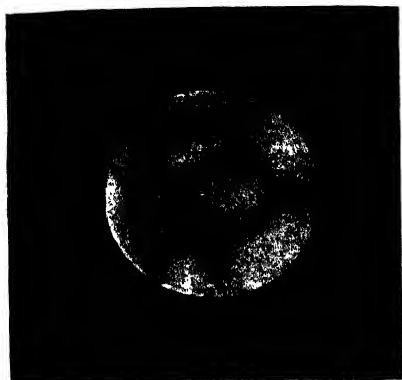


Fig. 1.



Fig. 2.

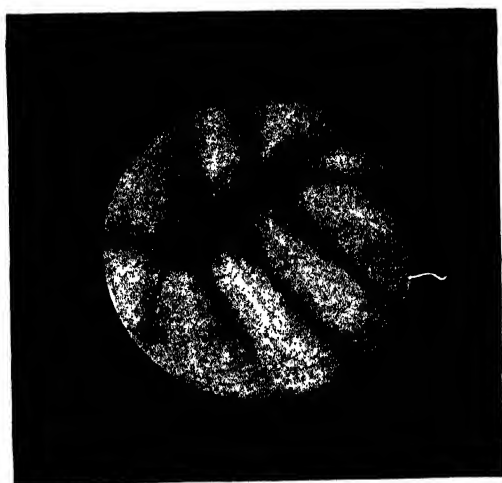


Fig. 3.

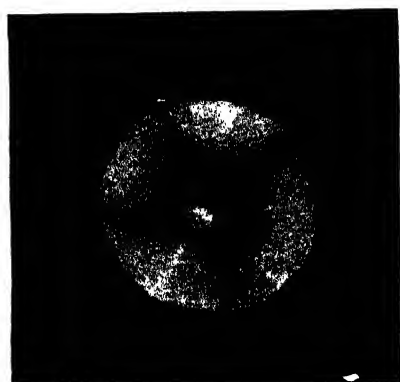


Fig. 4.



Fig. 5.

# Esophagoscopy and Gastroscopy in Cancer of the Esophagus and Stomach.

(H. H. Jancway and N. W. Green.)

Fig. 1, epithelioma in lower third of esophagus. Fig. 2, cardiac carcinoma seen through the partially dilated cardiac sphincter. Fig. 3, carcinoma of cardiac portion of the stomach. Fig. 4, carcinoma some distance within stomach. Fig. 5, entrance to the pyloric region of stomach as viewed through an indirect telescope inserted three to four inches within stomach.



for example, having found but 13 cases out of 8298 deaths from carcinoma. This does not include, however, cancer of the cardiac end of the stomach, which is usually considered as cancer of the latter organ.

The esophagus, appears to be invaded but rarely by cancerous growth, for, out of a series of 722 cancers in all parts of the body, only 6 were found in the esophagus. It seems to enjoy a certain degree of immunity from neoplastic invasion in contrast with the organs lower in the alimentary tract. Zenker and von Ziemssen have collected reports of 5079 autopsies, of which 0.36 per cent. showed esophageal cancer and 0.25 per cent. were primary. W. T. Cummins (N. Y. Med. Jour., Feb. 15, 1908).

**Symptoms.**—Cancer of the esophagus is attended with progressive stenosis, as already stated under the head of STRICTURE OF THE ESOPHAGUS. In some cases, however, the facies of the patient and cachectic symptoms denoting the involvement of other organs are first to appear. Pain is marked early in the cases; later on the tissue destruction involves the nervous supply, and the pain is no longer experienced. Slight hemorrhages may occur at this stage, though streaks of blood may have already been noted in the vomited matter. The cancerous process is then apt to invade the surrounding organs,—the larynx, the trachea, the bronchi and the lung, the pleura, the pericardium, and the larger vessels,—causing fatal hemorrhage. The cervical glands are often enlarged. The vertebrae may be included in the destructive process and involvement of the cord, with paralytic symptoms, appear. Paralysis of the larynx may also occur through pressure on the recurrent laryngeal. Progressive emaciation

begins early in the history of the case and death from exhaustion finally supervenes.

In 78 of the 104 cases of cancer of the esophagus reported, progressive difficulty in swallowing was the first sign of trouble. There was no pain in 61 cases, but in 5 cases pain preceded the dysphagia by a few days and in 11 cases they came on together. In 29 cases there was no pain until a month or two after the difficulty in swallowing had developed. In 19 of the 40 cases with pain it occurred only while food was being swallowed; in the others it was continuous. Regurgitation was the rule; it was absent in only 17 of the total 104 cases. The appetite remained good in 70 per cent. and there was distaste for meat in only 4 cases. The cancer proved fatal in most cases between six and twelve months, but in a few, in from two to four months.

Cancer is differentiated from spasm of the esophagus by the rapid sequence of the disturbances, gastrostomy becoming necessary in from one to four months, while spasm of the esophagus may persist for years without requiring this. Copious salivation and mucous vomiting are aids in diagnosing. In 1 case a woman of 28 had an evident spasm of the esophagus, but its persistence, notwithstanding great fluctuations, indicated an underlying organic lesion, confirmed by direct visual inspection and death in 5 months. L. Lanny (Arch. des mal. de l'app. digestif, Aug., 1910).

Carcinoma of the esophagus, in a case reported by the writers, gave practically no symptoms until a short period before death. A fistula between the esophagus and bronchus had existed for some time, food passing into the latter and finally causing bronchiectasis. This, in turn, caused small pulmonary hemorrhages and cough, thus simulating tuberculosis. Guttman and Held (Med. Rec., June 10, 1916).

Laryngeal crises and paroxysms of dyspepsia in a man of 75 years suffer-

ing from cancer of the esophagus were accompanied by a rapid rise in blood-pressure. **Venesection** brought the blood-pressure down at once, at the same time that it relieved the suffocation. Harvier and Bariety (*Bull. de la Soc. méd. des hôp.*, Feb. 6, 1925).

**Diagnosis.**—Progressive stenosis is a feature of all cases of stricture; hence the diagnosis must be based upon other symptoms. When the facies of the patient, a family history of cancer, and absence of local injury, syphilis, or tuberculosis can be recorded in a patient aged over 40 years, the likelihood that cancer is present is very great. Ejecta of portions of the mass will then reveal the characteristic histological features of cancer.

In cancer of the upper third of the esophagus the author has found what he terms progressive retrofixation of the tongue to be a very early and characteristic sign. The tongue cannot be protruded by the patient more than a few centimeters without his feeling pain, and when the examiner exerts traction on the organ an unusual degree of resistance is noticed. This sign was not observed in cases of functional spasm, tuberculosis, or syphilis of the esophagus, even at an advanced stage of the disease. Guarnaccia (*Arch. intern. de laryn., d'otol.*, etc., July-Aug., 1912).

The writer advocates endoscopic examination in cancer of the esophagus, but warns that before any person is thus examined it is important to study the esophagus by means of fluoroscopy or röntgenoscopy to exclude aneurism and to observe any departure from the normal function or obstruction in the passage of the barium meal through the esophagus. E. J. Patterson (*Penna. Med. Jour.*, Dec., 1919).

In the majority of cases, however, such clear signs cannot be obtained. Then pressure from a growth ex-

ternal to the esophagus must be excluded; an aneurism, an enlarged gland, etc., may, as shown, cause stricture. If the stenosis is near the larynx it is rarely cancer, but a cicatricial stricture or an impacted foreign body. The auscultation test described may be employed, and also the esophageal bougie, but the latter must be used with extreme care.

Cancer of the esophagus can usually be readily diagnosed by the history and by sounding, but it is much more difficult to diagnose cancer of the cardia in an early stage. Esophagoscopy, however, is of the greatest importance both in cancer of the esophagus and in cancer of the cardia, besides X-ray examination. The annexed colored plate clearly illustrates the diagnostic value of esophagoscopy.

The diagnosis can be established by radioscopy and esophagoscopy. The radioscopy signs deduced from the test-meal examination of 142 cases were: (1) A permanent stoppage of the bisnuth varying according to the degree of the obstruction in the esophagus; (2) a more or less marked dilatation, sometimes rather slight, above the stenosed part; (3) presence of dilatation, more or less fusiform, not exceeding the width of four fingers, followed by a narrow rectilinear or sinuous passage. Early and progressive dysphagia is the most important and frequent symptom of esophageal cancer. F. de Maraes Sarmiento (*Arch. d. mal. de l'appareil digest.*, ix, 71, 1916).

As urged by the writer, there are only 2 safe, certain and early methods of diagnosis of cancer of the esophagus—roentgenoscopy and esophagoscopy. There is good reason for the belief that when every patient with supposed "globus hystericus" or with the slightest subjective abnormality in swallowing is promptly examined with

the esophagoscope, the thoracic surgeon will show a good percentage of cures. Chevalier Jackson (*Arch. of Surg.*, Jan., 1926).

**Etiology and Pathology.**—Almost all cases of cancer encountered in the esophagus are of the squamous-epithelioma variety, the growth starting from the pavement epithelium of the mucous membrane, most frequently in that of the lower third of the organ. It gradually invades the mucous membrane, and, progressing laterally, the lumen of the cavity is soon reduced by a ring-like neoplasm. Later, the deep tissues become involved and the epithelioma, if the patient lives long enough, may extend to any of the important organs of the thoracic cavity.

Cancer occurs especially in males over 40 years of age. An inherited predisposition and an exciting cause—such as prolonged use of alcohol, strong condiments, hot fluids, or an ulcer—are thought to afford the necessary conditions for its development.

**Treatment.**—Radium has in recent years given a proportion of favorable results which warrants further use of this method.

The writer used 50 mgm. of radium in 11 cases and obtained prompt relief of dysphagia and gain in weight in many instances. The results were not reflected, however, by a reduction of the esophageal deformity and stenosis commensurate with the functional improvement. In several cases slight dysphagia returned, but usually it was relieved by another treatment. Mills and Kimbrough (*Jour. Amer. Med. Assoc.*, lxxiv, 1570, 1920).

A radium applicator consisting of a silver tube 2 centimeters long, containing 40 mg. of radium element and suspended by a stout thread, was used by the writer. The usual exposure was

for about 11 hours, about every ninth day. In 3 out of 6 cases the eating capacity was restored and exploratory excision showed no further trace of the cancer. Suter (*Deut. Zeit. f. Chir.*, Apr., 1921).

Radium applications to the upper esophagus may be made through the esophageal speculum, or lower down by the esophagoscope. The writer has used the **radium needle**, giving off both the beta and gamma rays, as well as the protected or **screened tube**, supplying the gamma rays alone. H. H. Forbes (*Boston Med. and Surg. Jour.*, May 25, 1922).

The writer employs **radium seeds**, i.e., minute glass capsules each containing 1 to 3 millicuries, introduced 1 cm. apart in the tumor with the aid of esophagoscopy. There were no cures, but in most cases definite palliation for 3 or 4 months. D. C. Greene (*Boston Med. and Surg. Jour.*, May 25, 1922).

In 19 of the writer's 41 cases the outlook seemed to be favorable after radium treatment, but all have died since except 2; 1 of these, a man aged 67, is in excellent health 2½ years since the radium treatment. He had noted the first symptoms about 6 months before treatment was begun. Wassink (*Nederl. Tijdsch. v. Geneesk.*, Feb. 20, 1926).

Six patients with cured cancer of the esophagus. Swallowing had been more and more difficult until it became impossible. Under radium treatment, deglutition became normal and the malignant tumor completely healed. In 2 the recovery has persisted for 14 years. One of them, a physician, celebrated recently his 80th birthday. Other cases date from 2 to 13 months. An improvement in ability to swallow was manifest after 1 or 2 applications. At least 0.1 Gm. (1½ grains) of **radium bromide**, in 2 or 3 tubes, end-to-end, was applied every second day for 10 or 12 hours, to a total of 5 or 6 applications. A long catheter should be used for introduction of the radium into the esophagus. The tubes should cover the whole area of the stenosis,

and the filters should be thick, to arrest the secondary rays. Complete impermeability, metastases, paralysis of the laryngeal nerve and cachexia are contraindications for the radium treatment. Guisez (Bull. de la Soc. méd. des. hôp., Jan. 8, 1926).

Feeding by the mouth can be carried on for some time through the esophageal tube, but the insertion of the latter becomes increasingly dangerous, especially if any force is used, as ulceration increases, since it may find its way through the diseased area, and direct the food into the pleura or mediastinum, with prompt fatal result. **Rectal feeding** should therefore be begun early, especially when signs of ulceration are present.

The **diet** should be regulated according to the stage the cancer has reached. When ordinary food can no longer be swallowed, meat finely scraped, hashes, soft rolls, besides the usual semiliquid foods, such as mashed potatoes and milk, rice pudding, etc., should be given as long as possible to sustain strength. When even hashed or scraped meat cannot be endured, eggs may be used in increased quantities, raw or soft-boiled, to compensate for them. Then the diet should be exclusively liquid or semiliquid, using the catheter—very carefully introduced—if need be. A feeding instrument described by Delavan many years ago is very useful. It can be made with an ordinary soda-water bottle. Rectal feeding should be resorted to when all these measures fail to nourish the patient adequately. The mouth-washes are very useful in these cases and should be used frequently, and solutions of **cocaine** gradually increased from 4 to 10 per cent. in strength, if needed,

used with the atomizer before each meal to prevent pain during deglutition. **Morphine** should be used freely in these cases when they become hopeless, or if surgical procedures offer no reasonable chances of recovery.

The dysphagia is greatly aided by the use of the following pastils, according to Thomas:—

℞ *Cocaine hydrochloride* ..... 0.0025 Gm. ( $\frac{1}{25}$  gr.).  
*Morphine hydrochloride* ..... 0.005 Gm. ( $\frac{1}{2}$  gr.).  
*Antipyrin* ..... 0.10 Gm. ( $1\frac{1}{2}$  gr.).  
*Sugar* ..... 0.30 Gm. (5 gr.).

One or two of these pastils should be taken before each meal.

As an alternative prescription the following is recommended:—

℞ *Dionine hydrochloride*,  
*Codeine hydrochloride* ..... of each 0.10 Gm. ( $1\frac{1}{2}$  gr.).  
*Cocaine hydrochloride* ..... 0.25 Gm. (4 gr.).  
*Ammonium valerianate*,  
*Bitter-almond water*,  
of each ..... 7.50 Gm. (2 dr.).

Of this solution, 15 drops should be taken three or four times a day.

When the descent of food is hindered in cancer of the esophagus, Liebermeister recommends that the patient sip hourly small amounts of **hydrogen peroxide** solution (1 to 2 per cent.). A cleansing of the cancerous surface occurs which is sufficient to allow passage of food.

There should be given orally only such food as will readily pass through the stenosis. The treatment with **hydrogen dioxide** is to be maintained for weeks and months. When the stenosis is absolute the patients are to receive nourishment by rectum and

only the hydrogen dioxide solution by mouth for two or three days; the administration of fluid food may then be begun and will be found possible in most cases. If even then no fluid will pass through the stenosis, the patient receives subcutaneously 0.01 Gm. ( $\frac{1}{60}$  grain) of **morphine**, or 0.001 ( $\frac{1}{600}$  grain) of **atropine**, or half of this dose in combination, half an hour before the time for meals, three times a day for several days. The introduction of sounds should be considered a last resource, of which use should be made only in exceptional cases.

If the malignant growth is located at the junction of esophagus and the pharynx or stomach, **surgical removal** may prolong life.

The writer urges **early operation** before the tumor has involved tissues outside of the esophagus, and while the patient's general health is fairly good. Torek (Arch. of Surg., Jan., 1926).

Some progress in radical esophageal surgery is gradually being made. In **reconstruction of the esophagus** the stomach is separated from its omentum, drawn up under the skin of the chest into the cervical wound, and an anastomosis of the stomach made with the cervical stump of the esophagus, all the diseased portion of which has already been removed after separation from its bed and division at its cervical end. The function of the esophagus is thus taken over by a tube-like process of the stomach, and the food passes down over the chest-wall instead of within. Lotheissen (Beitr. z. klin. Chir., cxxvi, Nos. 2-3, 1922) has tabulated 45 cases of completed and 44 of uncompleted plastic operation for esophageal stenosis. Among the 45 the stomach was used in 17 cases and the jejunum instead in 25. In addition, there are 41 cases of plastic operation for esophageal cancer, but the procedure was completed in only 1, and the patient died soon after. The writer has himself used the stomach method in 4 cases

of stenosis due to lye, with permanent success in 2; in all, the stomach plastic served its functional purpose. Kummel (Arch. f. klin. Chir., Nov. 17, 1921), to reduce the chances of infection in the stomach procedure, first draws the stomach up in place of the esophagus in the posterior mediastinum, so that the resection of the carcinoma can be done with the affected tissues outside of the body.

Another procedure sometimes followed is the formation of a subcutaneous tube of skin in front of the chest wall; when this is definitely established, the stump of the esophagus is connected with its upper end and the stomach with its lower end, either directly or through a piece of colon displaced for the purpose. Fonio (Schweiz. med. Woch., Dec. 29, 1921) reported a successful case of this form of **antethoracic esophagoscopy** in a long-standing case of corrosion by potassium permanganate. He has worked out a plastic "swallowing mechanism" that renders unnecessary the peristaltic action of the connecting portion of colon, which can thus be dispensed with.—Ed.

### NEUROSES.

**Spasm of the Esophagus (Esophagismus).** — *Symptoms.* — Spasmodic contraction of the muscles of the esophagus comes on suddenly, several attacks occurring in quick succession or intermittently, efforts to suppress them by swallowing saliva or food usually bringing them on. Deep-seated, cramp-like pain is usually experienced. Food on its way down to the esophagus may be regurgitated if still near the larynx; if below this it is retained *in situ* until the spasm has passed. The attacks may last but a few hours and recur only after months' intervals; again, they may be persistent and render proper alimentation impossible without recourse to auxiliary means. Solids can, as a rule, be swallowed.

True spasm as the result of organic disease of the nervous system is con-

sidered a rare condition; whereas functional spasm is of frequent occurrence and sometimes responsible for secondary lesions of a gross nature. Hill (Jour. laryn., rhin., and otol., Feb., 1912).

**Diagnosis.**—The constriction usually occurs near one of the extremities of the esophagus, but it may not be limited to these regions in succeeding attacks. Hysteria and other neuroses can usually be detected, especially in females, for whom the disease shows a predilection. The bougie may be used advantageously to distinguish esophagismus from the organic lesions already described. In spasm the instrument will encounter a stenosis during the active stage and pass down freely while no spasm is present.

**Etiology.**—Spasm of the esophagus is the manifestation of a general neurosis, particularly hysteria, and is therefore observed in young females. It may occur as a symptom of tetanus, rabies, epilepsy, chorea, and other neuroses, and as a result of violent emotions,—fright, joy, etc. It may also be associated reflexly with pregnancy, and with disorders of the genital system, or of other organs, especially the neighboring ones,—the pharynx and the stomach. It often attends the various organic diseases of the organ itself.

**Treatment.**—Treatment should be directed to the symptoms. The painful deglutition, inability to swallow solids, and the choking sensation are usually promptly relieved by the passage of the **esophageal sound**, the moral effect adding its share to the good result. Sometimes, however, this procedure increases the spasms. Inhalations of **nitrite of amyl**, by relaxing all vessels, diminishes the

volume of blood supplied to esophageal muscles, and, therefore, their tendency to spasm. The **bromides**, or rectal injections of **chloral**, 15 grains (1 Gm.), in free solution, can be used for a similar purpose. In some cases the spasms are kept up by nasopharyngeal catarrh and cease when this condition is properly treated. Antispasmodics, such as **camphor** and the valerianates, especially the **zinc valerate**, are sometimes useful. An **emetic** sometimes proves efficacious, especially when, as sometimes occurs, the cause of the spasms, a foreign body, is brought up. A **cocaine spray**, using a 5 per cent. solution, before meals, is useful to facilitate the ingestion of food and its retention. In some hysterical cases **suggestion** will alone prove useful. The patient, for instance, may be suspended by the arms to a cross-beam and kept there some time, with the verbal assurance that on being freed her spasms will cease.

**Paralysis of the Esophagus.**—**Symptoms.**—Paralysis of the esophagus is rarely met with. There is functional inactivity of the muscular coat of the esophagus and great difficulty is experienced in swallowing, the bolus remaining *in situ* if at all large. Liquids pass down with ease and are used by the patients to “wash down” small masses of solid food. The accumulation of food in the esophagus often engenders dilatation, and the symptoms of the latter disorder are the predominating ones.

**Etiology.**—Paralysis of the esophagus is usually due to extensive bulbar paralysis and other central nervous disorders. But it may also occur in a complication of peripheral disorders, especially diphtheria, en-



larged lymphatic glands, and of syphilis, alcoholism, plumbism, etc.

**Treatment.**—The treatment indicated is that of the causative disorder. In diphtheric paralysis **arsenic** is most effective. After a course of this remedy hypodermic injections of strychnine are often effective. **Faradism**, the negative pole in the sulcus directly in front of the sternomastoid and the positive back of the neck, may be simultaneously employed.

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Philadelphia.

**ETHER (sulphuric ether).**—C. W. Long, in 1842, was the first to employ ether as an anesthetic in surgical operations, though to C. T. Jackson, a chemist, and W. G. T. Morton, a dentist of Boston, belongs the credit of securing for it general recognition (1846).

Ether ( $\text{H}_3\text{C.H}_2\text{C.O.CH}_2\text{CH}_3$  or  $(\text{C}_2\text{H}_5)_2\text{O}$ ; specific gravity, 0.716 to 0.717 at 77° F.) is chemically diethyl oxide and is obtained by the gradual addition of 90 per cent. alcohol to heated (140° C.) concentrated sulphuric acid, which combines with a portion of the alcohol present to form ethyl hydrogen sulphate ( $\text{C}_2\text{H}_5\text{H.SO}_4$ ); the latter, in turn, reacts with the remaining alcohol to form ether, which is distilled off and then purified by shaking with water and an alkali, and redistillation.

Ether appears as a colorless, mobile liquid, having a characteristic, penetrating odor, generally regarded as pleasant, and a sharp, burning taste. It is much more soluble in water than is chloroform—1 in 10 or 12 instead of 1 in 200—and mixes in all ratios with alcohol, chloroform, benzene and fixed and volatile oils. Pure

ether will take up water to the extent of 1 part of the latter in 35 parts of ether.

It is very volatile, evaporating more rapidly than chloroform at ordinary temperatures, and has a much lower boiling point—96° F. (35.5° C.) instead of 140° F. (60° C.) in the case of chloroform. Ether vapor is heavier than air, and since it is very inflammable, its use for anesthetic purposes in the presence of artificial light other than incandescent electric bulbs is attended with danger, unless the light be placed at a considerable distance above the patient. A mixture of ether vapor and air, when ignited, explodes violently.

Ether is officially permitted to include about 4 per cent. of alcohol, the latter containing, in turn, a little water. The alcohol has been generally considered to act as a preservative for ether, but more recently this has been shown to be an error. The presence of alcohol in ether is of no value except where the anesthetic is given by the drop method, when the alcohol obviates excessively rapid volatilization of the ether and consequent chilling of the apparatus employed (Baskerville).

Impurities in ether may depend either upon the use of unsuitable alcohol in its production—*e.g.*, ethyl alcohol denatured by methyl alcohol, when the product obtained will be an ethyl ether mixed with methyl or methyl-ethyl ether ("methylated ether"), or upon the addition of impure ethyl alcohol to a pure ether for the doubtful purpose of rendering it more suitable for anesthetic use, or, again, upon the formation of adventitious substances, partly owing to improper storage of the originally

satisfactory ether. Prolonged exposure of ether to light and air may result in the production, during anesthesia, of such symptoms as coughing and suffocation, as well as serious after-effects.

According to Cotton (Can. Med. Assoc. Jour., Sept., 1917) and Wallis and Hewer (Lancet, June 4, 1921), pure ether is devoid of anesthetic properties, the action of commercial ether being due to impurities such as carbon dioxide, ethylene, and ketones. A later investigation by Stehle and Bourne (Jour. Amer. Med. Assoc., July 29, 1922), in which ether made by a clean-cut chemical reaction, practically excluding the ordinary impurities, was used, disproved the conception of the preceding observers.

Rowe (Jour. of Pharmacol. and Exper. Ther., Apr., 1923) recalls that the pharmacopœias of the world specify that aldehyde and peroxide are not permissible in anesthetic ether. Over one-third of the high-grade anesthetic ether on the market today contains appreciable amounts of one or of both of these substances. All anesthetic ethers should be analyzed as a matter of routine, to preclude the presence of these deleterious materials.

A colorimetric method based upon fuchsin has been devised for the exact determination of the aldehyde content in anesthetic ethers. The titrimetric method, using cadmium potassium iodide in acid solution and sodium thiosulphate, has been devised for determining the peroxide in ether.

Evidence is available showing that the type of container is a factor in the contamination of ether initially pure, and that the metal of the container exercises a definite catalytic action on the oxidative reaction producing the impurities.

Studies made by Ronzoni, Koechig and Eaton (Jour. Biol. Chem., Sept., 1924) indicate that accumulation of lactic acid accounts in a large part for the acidosis of ether anesthesia. Its increase is independent of carbon dioxide tension and produces the changes in  $pH$  rather than being itself controlled by  $pH$ , as stated by Anrep and Cannan. Decreased oxygen supply to tissues does not account for its production. The source of lactic acid seems to be the

muscle tissues. Production of lactic acid in the muscle, together with loss of phosphate from the muscle (Stehle and Bourne), during anesthesia, points to a breakdown of some hexose phosphate, such as Embden's "lactacidogen."

Aldehyde in ether may be detected by occasionally shaking 10 c.c. of ether in a test-tube, during one hour, with 1 c.c. of a 6 per cent. solution of potassium hydroxide in water. Neither of the liquids should show any coloration at the end of the hour; otherwise aldehyde is present (U. S. P.). Undue acidity of ether may be tested for by dipping blue litmus paper, moistened with water, into ether for ten minutes. No residue or foreign odor should be left when ether is allowed to volatilize from an evaporating dish or from odorless blotting paper.

#### PREPARATIONS AND DOSES.

—In addition to its uses as an anesthetic, ether is sometimes administered internally. Its preparations are:

*Æther*, U. S. P. (ether), required to contain 96 to 98 per cent. of absolute ether, the remainder consisting of alcohol and water. Dose, 10 to 60 minims (0.6 to 4 c.c.).

*Spiritus ætheris*, N. F. (spirit of ether; Hoffmann's drops), composed of 32.5 parts by volume of ether and 67.5 parts of alcohol. Dose,  $\frac{1}{2}$  to 2 fluidrams (2 to 8 c.c.).

*Spiritus ætheris compositus*, N. F. (compound spirit of ether; Hoffmann's anodyne), consisting of 32.5 parts by volume of ether, 2.5 parts of ethereal oil ("heavy oil of wine"), and 65 parts of alcohol. Dose,  $\frac{1}{2}$  to 2 fluidrams (2 to 8 c.c.).

[The B. P. recognizes two sorts of ether: (1) *Æther*, only required to contain 92 per cent. by volume of pure ether, and (2) *Æther purifica-*

tus, or ether freed from most of the alcohol and water, and having a specific gravity of 0.720.]

### PHYSIOLOGICAL ACTION.—

Rapid absorption of ether takes place in the lungs when its vapor is inhaled, as it is possessed of a high vapor tension and penetrates the tissues with great facility. All mucous membranes absorb it promptly, and the same physiological effects may be secured—though more slowly—by its ingestion as by the customary route of administration. Locally, it causes temporarily a pronounced irritation of the sensory nerve-endings and vessel-walls, followed by a dulling of sensibility. It is less irritating, volume for volume, however, than chloroform, though in practice this difference is more than counterbalanced by the fact that a much larger amount has to be introduced than of chloroform to produce an equal general anesthetic effect.

The type of patient in war is different from that in a general hospital in peace time. Most of the patients are robust young men living an out-of-door life. Those with shell shock require much more anesthetic and have a greater tendency to excitement while going under its influence. T. Clarke (*Brit. Med. Jour.*, i, 79, 1918).

That ether, like chloroform, is capable, in sufficient concentration, of paralyzing the life processes in any form of cell is illustrated in that it arrests the streaming of the protoplasm in plant cells, as well as the activity of the cilia in the ciliated epithelia of animals. If its action be soon discontinued, recovery of function occurs; but where it is kept up for a certain minimal period, cellular death takes place. Thus under the

prolonged direct influence of ether the irritability of nerve-tissue is permanently lost, rigidity of muscle-tissue supervenes, and the red blood-cells are destroyed.

Rapid evaporation of ether is accompanied by a sudden and marked absorption of heat, which is easily capable of inducing a fall in temperature in adjacent bodies to below the freezing point. This is the chief factor in the production of local anesthesia with ether, though direct paralysis of the terminal nerve-filaments and endings by the anesthetic itself may also play a part.

**Nervous System.**—The characteristic general anesthetic action of ether is due, according to the Meyer-Overtton theory, to its dissolution in the lipoids or complex fatty substances of the nerve-cells, the function of which is thereby temporarily interrupted, through loss of the normal relationships of the lipoids to the remaining cell-constituents. The reason for its accumulation in these—and other—fats is that it is more soluble in these fats than in the water of the blood itself. In the beginning of anesthesia, at least, the blood returning to the right heart from the general circulation contains less ether than that entering the left heart from the pulmonary circulation, for the anesthetic has been taken up from the blood by the various fatty tissues it has reached in its systemic journey. At no time, however, does the blood completely give up its ether to the fats; the condition present at the height of anesthesia is one in which the ratio of the ether present in the blood and fats corresponds with the relative solubilities of ether in these two dif-

ferent media. Rises and falls in the ether content of the blood are soon paralleled by proportionate rises and falls in the nervous tissues. Once a sufficient degree of anesthesia is attained, the amount of ether to be supplied is approximately only that which will maintain a sufficient percentage of the gas in the air-cells to balance that in the blood and prevent any of the ether in the blood from being re-excreted. The depth of anesthesia in any given period depends not only upon the amount of ether that has already been introduced into the organism and reached the nerve-tissues, but upon the percentage of ether in the inspired air. As soon as the air-ether mixture is diluted to a certain degree, ether begins to pass out from the blood and the percentage of ether in the expired becomes greater than it is in the inspired air.

Ether differs from chloroform in that its effect appears more slowly, in the greater concentration of vapor required to bring about anesthesia, and in the greater margin of safety, *i.e.*, the greater difference between the concentration of vapor which will just bring on anesthesia and that which will cause death. Thus, Nicloux showed in dogs that whereas, in deep chloroform anesthesia, the percentage of the anesthetic in the blood averaged 0.05 per cent., that of ether under the same conditions was 0.13 to 0.14 per cent. Again, whereas Rosenfeld showed in rabbits that a 3.5 per cent. ether vapor is required to bring on complete anesthesia by inhalation and a 6 per cent. ether vapor must be used to cause respiratory arrest, Spenser found that the corresponding figures in the

case of chloroform are approximately 1.0 and 1.6 per cent. At least 3 times as great a percentage of ether as of chloroform in the inspired air is required for anesthesia (Gottlieb).

The action of ether on the nervous system is similar to that of chloroform and of large amounts of alcohol consisting in a progressive paralysis of various brain centers, sometimes preceded by a short stage of stimulation.

Sajous has noted marked decrease of mental activity in dementia precox following the use of ether as anesthetic. Lecithin, a constituent of the brain cells, is known to be dissolved by ether. The sensory centers are affected first, then the motor, the morbid process then passing downward.

Experiments with animals have constantly demonstrated that the anesthesia can be shortened or suspended altogether if a suspension of lecithin is injected intravenously soon after the induction. Nerking (*Munch. med. Woch.*, Aug. 18, 1908).

The ether concentration reached in the central nervous system [rich in lecithin], not that in the body as a whole, is the determining factor in the anesthetic action of ether. Haggard (*Jour. Biol. Chem.*, Apr., 1924).

A circumstance sometimes overlooked is that even before consciousness and tactile sensation have been completely lost, analgesia may be present. In deeper anesthesia, the centers of consciousness and other brain centers become entirely paralyzed, and finally the spinal cord is involved, the reflexes disappearing and the muscles finally completely losing their tonicity. The functions of the respiratory and vasomotor centers, however, are not endangered until a still larger quantity of the

drug has been introduced, and the art of anesthesia consists in avoiding encroachment of the effects of the drug on these centers, while maintaining the action on the receptive and motor nuclei.

**Circulation.**—The heart rate is always increased in ether anesthesia, often to 90 or 100 per minute. This effect is due, at least in large part, to direct or reflex actions on the extracardiac governing centers of the heart, since it is wanting if the nerves to the heart have been cut. There has been produced no evidence to the effect that ether directly stimulates the heart muscle (Gottlieb), though the vasoconstrictor action of ether, by increasing the blood-pressure, may result in a better supply of blood to the heart.

The peripheral vessels of the skin, especially in the face, are dilated by ether. This effect is different from that of chloroform in that it persists during the anesthesia, the skin remaining flushed throughout, whereas with chloroform the flush tends to give way gradually to pallor. The splanchnic or internal vessels, on the other hand, are constricted by ether, probably owing to an action both on the vasomotor center and the vessel themselves. This vasoconstriction more than offsets the simultaneous peripheral vasodilatation, and in conjunction with the increased heart rate causes an increase in the blood-pressure, which generally persists throughout the anesthesia, when the latter is not prolonged. Such a rise in pressure, more or less marked, is an almost constant accompaniment of ether anesthesia. The effect of chloroform differs in that there is a tendency to direct depression of the heart

and splanchnic vessels, and the blood-pressure gradually falls during anesthesia. In perfusion experiments chloroform has shown itself to be about 35 times as depressing to the heart muscle as ether. Only after prolonged deep ether anesthesia does the heart become depressed and the splanchnic circulation relaxed.

Reflex fatal cardiac inhibition, through irritation of the trigeminal terminals in the upper respiratory passages and transmission of the impulse to the vagi, is far less likely to occur with ether than with chloroform: (1) because the direct depressing action of the drug on the heart is far less than in the case of chloroform, the cardiodepressing action of which strongly predisposes to inhibition of the heart, and (2) because of the wider latitude in the concentration of the vapor administered in the case of ether.

**Respiration.**—Ether tends to stimulate the respiratory center, probably both directly and through excitation of the afferent vagal nerve-paths from the lungs. The breathing is at first accelerated and deepened. In the stage of excitement it becomes irregular. In the narcotic stage, however, it is regular again and slightly slowed, afferent impulses no longer exciting it owing to the general sensory paralysis.

Where the ether is pushed beyond the stage of anesthesia proper, the respiratory movements may gradually dwindle in their amplitude until arrest occurs, or they may come to a standstill more or less suddenly. Respiratory paralysis by ether usually occurs at a time when the heart is still capable of maintaining a good circulation, and recovery is usually

readily secured by artificial respiration. With chloroform, on the other hand, the heart is already considerably depressed when the breathing ceases and artificial respiration is not as effectual as under ether.

**Blood.**—Like chloroform, ether, when circulating in the blood, is present in greater concentration in the red blood-cells than in the plasma, owing to the lipoids present in the former. In high concentration it readily produces hemolysis. In the course of ordinary ether anesthesia, a slight, temporary decrease of the hemoglobin in the blood has been shown to take place.

It is urged that whenever possible one or two blood examinations be made before preparation of the patient for etherization. Less than 50 per cent. of hemoglobin indicates that an anesthetic is dangerous and only allowable in vital emergencies. J. Chalmers Da Costa and J. L. Kalteyer (Boston Med. and Surg. Jour., June 13, 1901).

Ether causes a marked decrease in the coagulation time, most marked from the seventh to the tenth days. Nitrous oxide causes no permanent effects of any significance; ether causes more harmful changes, while chloroform causes the most harmful results (hemolysis and production of distinct anemia). Hamburger and Ewing (Jour. Amer. Med. Assoc., Nov. 7, 1908).

Report of experiments made to determine the effects of ether on the phenomena of bacteriolysis, agglutination, and phagocytosis. The reduction of the phagocytic powers of blood after an ordinary ether anesthesia in different experiments lasted from two days to several weeks and was due apparently to a direct effect on the leucocytes and serum without any action on the bacteria. A very small addition of lecithin *in vitro* restored the phagocytosis. E. A. Graham

(Jour. Amer. Med. Assoc., March 26, 1910).

The catalase content of the blood decreases during the administration of ether and increases during the recovery from ether. The decrease is due to the destruction of catalase by ether, the increase to an increased output of catalase from the liver. The decrease in catalase during the administration of ether may be the cause of the decreased oxidation during anesthesia, while the increased output of catalase from the liver during recovery may account for the increased oxidation during this period. Burge (Amer. Jour. of Physiol., Oct., 1917).

Both ether and chloroform anesthesia, when prolonged for over 30 minutes, were accompanied by a distinct lowering of the alkali reserve of the blood. It was probable that this mild transient acidosis was a most important factor in the production of post-operative vomiting. The alkali reserve of the blood could be increased by the administration of **sodium bicarbonate**, and it was, therefore, a most rational procedure to use this drug as a preoperative prophylactic measure against excessive post-operative vomiting. G. B. Wood (Trans. Amer. Laryn. Assoc.; N. Y. Med. Jour., Dec. 29, 1917).

The advisability of pre-operative blood study was also illustrated in a case in which profuse oozing of blood required 1 hour for its control after the operation. The blood taken before operation had shown an almost complete absence of blood platelets. In such cases **calcium chloride**, 1 dram (4 Gm.) 4 times daily, should be given for 2 or 3 days before operation. A platelet count below 200,000 indicates a predisposition to hemorrhage. M. G. Day (Amer. Jour. Surg., Apr., 1922).

In dogs ether anesthesia decreased the rate of epinephrin output from the suprarenal glands. Kodama (Tohoku Jour. Exper. Med., Mar. 28, 1924).

**Temperature.**—During anesthesia a gradual fall in temperature occurs,

owing to the dilatation of the skin vessels, which accelerates heat loss, and muscular inactivity, which results in diminished heat production. The anesthetic is, in addition, believed to depress the heat centers. In advanced stages of narcosis, another factor favoring low body temperature is introduced when circulatory activity becomes impaired.

Chloroform produces a loss of body temperature approximately equal to that produced by ether. Warming the ether vapor before inhalation will prevent the loss of body temperature, or may actually increase it in a degree proportionate to the temperature of the vapor and also to that of the operating room. Patients should not only be kept dry and warm, but be anesthetized in a room free from draughts, and should not be transferred to a cold room. Davis (Bull. Johns Hopkins Hosp., April, 1909).

**Metabolism.**—Some metabolic processes are slowed during anesthesia, but on the next day there is observed an increased elimination of nitrogenous waste-products in the urine. The urea excretion, however, is subnormal, while ammonia and uric acid are increased; this shows that the products of cell metabolism have been only imperfectly broken down.

In ether narcosis depression of oxidation processes occurs. Experiments show that even with a free supply of oxygen a fatigued ganglion cell does not recover at all during narcosis. There occurs, rather, a gradual asphyxia, —although this process is only developed to a small extent in light narcosis. M. Verworn (Bull. Johns Hopkins Hosp., April, 1912).

The increase in the  $\text{CO}_2$  output is accompanied by a narcotic change leading to death in animals, while this is not necessarily the case in plants. The narcotic action of ether on the animals studied was accompanied by

a decrease in the  $\text{CO}_2$  output; in plants this is not ordinarily the case. Irwin (Jour. Gen. Physiol., Nov., 1918).

There also occurs an increase in the sugar content of the blood—hyperglycemia—and some interference with the metabolism of fats, acetone and diacetic acid being not infrequently found in the urine.

Ether anesthesia produces a hyperglycemia both in the diabetic and the normal person. In the diabetic the risks run are due to anesthesia and shock, both of which produce hyperglycemia. The writer cites 5 cases to show that the same is true in the non-diabetic person. There is a definite relationship between this hyperglycemia, associated with ether anesthesia, and the toxic symptoms that follow. The treatment should be on lines used in diabetes. Pemberton and Cunningham (Lancet, Apr. 11, 1925).

**Elimination.**—Ether is eliminated unchanged, chiefly by way of the lungs, and very slightly through the kidneys and skin. Its excretion is distinctly more rapid than that of chloroform, this accounting for the fact that recovery from anesthesia occurs more quickly where ether is used than with chloroform. According to the experimental work of Nicloux, the elimination of ether is as complete in two hours after the cessation of its administration as in seven hours after chloroform. The relative insolubility of chloroform in the water of the blood as compared with ether (approximately 1 in 200 instead of 1 in 10) causes it to remain more steadfastly in the fatty tissues in which it is freely soluble, with the result that the elimination of the last traces of anesthetic is effected more slowly than in the case of ether.

#### ETHER AS AN ANESTHETIC.

—Ether possesses the following ad-

vantages over chloroform: Greater immediate safety; less likelihood of causing fatty degenerative changes in the parenchymatous organs; more rapid excretion of the drug. The first of these is the most important, and under most circumstances is of itself sufficient more than to offset numerous advantages of chloroform such as more rapid action, less likelihood of excitement during the induction of anesthesia, rarity of pulmonary complications, less flow of mucous secretions, etc.

Ether should be used as an anesthetic in **obstetric practice** when pulmonary complications are absent. Its action upon the uterine contractions in the second stage of **labor** is preferable to that of chloroform. No anesthetic should be given in the first stage of normal labor. Uterine atony and post-partum hemorrhage are rare following ether anesthesia. Ether should be used in **eclampsia** in preference to chloroform. Its action is as positive and the danger much less. It is safer to the mother than chloroform. The danger of delayed poisoning is slight. H. M. Stowe (*Surg., Gynec. and Obstet.*, Feb., 1910).

The author always administers ether in **thyroid cases** and in **trephining operations**, and has not noted any undue congestion or hemorrhage, which has so often been charged against ether as an anesthetic in these cases, and which, no doubt, does apply to any method where the air is restricted. Samuel Johnston (*Can. Pract. and News*, March, 1912).

The comparative safety of ether as an anesthetic has been amply shown by statistics. Those of Foy, based upon 877,507 chloroform administrations, show a mortality of 1 in 4301 for this anesthetic, while those of Julliard, based upon 314,738 ether administrations, show a mortality of only 1 in 14,987. Hewitt, combining

the figures of Julliard with those of Ormsby, and calculating from a total exceeding 1 million anesthetics, found a death rate of 1 in 3162 for chloroform and 1 in 16,302 for ether. The number of chloroform anesthetics has of late years shown a marked decrease in the United States.

Report of 112 responses to question blanks sent out to surgeons concerning their anesthetics during 1908. Chloroform was used in 20,613 cases, with 1 death to 2060; ether in 11,859, with 1 death to 5930; chloroform plus ether in 10,232, with 1 death in 3410; and the scopolamine-morphine mixed anesthesia in 23,809 cases, with 1 death in 4762. Local anesthesia or the first whiffs of ether were utilized in fully a quarter of all cases that would formerly have required general anesthesia, and no fatality was reported with these methods. Kummell reports only 0.61 per cent. of postoperative pneumonias in contrast to 2.5 per cent. formerly, and von Eiselsberg only 0.9 per cent. instead of 3.3 per cent. formerly. Neuber (*Archiv f. klin. Chir.*, Bd. lxxxix, Nu. 4, 1909).

The above figures probably give an incorrect idea, however, of the relative danger of chloroform anesthesia in warm climates, such as exist in the southern United States, and probably under certain other circumstances. Thus Lawrie has reported 30,000 chloroform anesthetics without a death, and Dastre reported only 1 death in 11,448 chloroform administrations during the Crimean war (Gwathmey). Chloroform with oxygen in a southern climate is considered by Gwathmey a very safe anesthetic; he thinks also that in the northern United States chloroform is safer in the summer than in the winter. The same author gives the following table showing the mortality of various anesthetics according to statistics obtained from 99 hospitals



in this country and including the years 1905 to 1911:—

Anesthetic.	Total of Anesthetics.	Number of Deaths.	Ratio of Deaths.
Local anesthesia .....	14,878	0	0-14,878
Nitrous oxide with oxygen ....	8,585	0	0-8,585
Anesthol-ether .....	3,827	0	0-3,827
Ethyl chloride .....	905	0	0-905
Nitrous oxide with air .....	561	0	0-561
Spinal analgesia .....	521	0	0-521
Anesthol-ether-chloroform ....	153	0	0-153
Anesthol-chloroform .....	123	0	0-123
Nitrous oxide-ether-anesthol ..	114	0	0-114
Essence of orange-ether sequence .....	100	0	0-100
A. C. E. or C. E. mixture .....	95	0	0-95
Ether-chloroform sequence ....	94	0	0-94
Nitrous oxide-anesthol .....	45	0	0-45
Ethyl chloride-anesthol .....	41	0	0-41
Anesthol-oxygen .....	37	0	0-37
Ethyl bromide .....	20	0	0-20
Ethyl-chloride-oxygen .....	13	0	0-13
M-H-C anesthesia .....	9	0	0-9
Chloroform-ether sequence ....	16,054	2	1-8,027
Nitrous oxide-ether sequence ..	41,435	6	1-6,905
Anesthol .....	6,139	1	1-6,139
<b>Ether, drop or vapor .....</b>	<b>157,453</b>	<b>28</b>	<b>1-5,623</b>
Ethyl chloride-ether sequence ..	4,431	1	1-4,431
Chloroform-oxygen .....	4,009	1	1-4,009
<b>Chloroform, drop or vapor ...</b>	<b>16,390</b>	<b>8</b>	<b>1-2,048</b>
Nitrous oxide .....	1,314	2	1-657
Rectal anesthesia .....	516	1	1-516
Intratracheal insufflation .....	1,000	4	1-250
Nitrous oxide-ether-chloroform ..	183	1	1-183
	278,945		

Of the eight chloroform fatalities shown in the table four occurred in the United States Army and the localities in which they took place are not known. Of the other four all occurred in a northern climate. Gwathmey concluded that chloroform is approximately  $2\frac{1}{2}$  times as dangerous as the nitrous oxide-ether sequence.

For routine work, ether, by the open or drop method, is the safest and most satisfactory anesthetic. In the usual run of cases it is the anesthetic of choice in from 75 to 80 per cent. of the cases. Possibly in a laryngectomy the direct introduction of chloroform vapor into the trachea might produce less irritation to the tracheal mucosa with less risk of pneumonia than ether. Bevan (Jour. Amer. Med. Assoc., Dec. 2, 1911).

None of us now know which is the better, the open or the closed method.

The gas-ether sequence and the drop method are pioneers that should now be methods of the past. The drop method is inaccurate. The writer has never seen a patient struggle under this method. All his patients have preliminary medication. About  $2\frac{1}{2}$  ounces (75 cc) of ether in an hour's administration, when absolute relaxation is obtained, cannot be approached by the drop method. J. T. Gwathmey (Jour. Amer. Med. Assoc., Aug. 5, 1916).

The writer induces anesthesia in 7 minutes; her patients never have coughing or strangling, because she gives plenty of air in the beginning, which does not lengthen the time required for giving the anesthetic. If concentrated ether is given, the patient will hold his breath. Only enough anesthetic should be given to keep the patient asleep. The operation will regulate the amount needed for this; at certain stages the patient must be kept more soundly asleep than at others. Nausea and vomiting are almost things of the past with the open method. She has never seen shock produced by an anesthetic nor is the rapid breathing which accompanies the rebreathing method observed in the open method of etherization. Excitement is not seen except in alcoholics; but that occurs, regardless of the method which is employed. Isabella C. Herb (Jour. Amer. Med. Assoc., Aug. 15, 1916).

A small quantity of **chloroform** added to ether, about 1 to 20, largely does away with the irritant effects of the latter upon the respiratory passages, makes anesthesia simpler in induction, and increases its safety by preventing the excessive depression of the chloroform and the excessive stimulation from ether. W. J. McCardie (Brit. Med. Jour., Apr. 21, 1917).

**CONTRAINDICATIONS. Respiratory Disorders.**—Numerous cases of pneumonia following the administration of ether have been reported, and

it is well known that ether causes decidedly more irritation of the respiratory passages, where inflammation of these is present, than chloroform. For this reason, ether is contraindicated in acute affections of the lower respiratory passages. In chronic disorders such as bronchitis, with profuse secretions, pulmonary emphysema, and tuberculosis, chloroform is preferable to ether, except where the heart is weak. Asthma, goiter, and all other conditions tending to reduce the lumen of the bronchial tubes or trachea are to be looked upon as compromising factors in ether anesthesia.

Ether is taken by young children very well for short operations if it is carefully given, but as the body temperature may be lowered from  $\frac{1}{2}^{\circ}$  to  $3^{\circ}$  F. very quickly, and that loss is very serious, one should hesitate before giving ether to a very young child. Some years ago the author tested the effects of giving ether to young children, and the main points which struck him were the liability to salivation and bronchorrhea, which he regarded as not only distressing, but injurious to the children. Buxton (*Proceed. Royal Soc. of Med.*, April, 1910).

To prevent secondary and late congestive phenomena in the lungs from the ether anesthesia with cold vapor, the writers advocate **warm ether vapor**. They pass the ether vapor through a bent tube plunged in hot water which is kept warm by a thermos bottle. They have practised this in 250 to 300 cases, and never have had any immediate accident, nor pulmonary complication. They have been able to continue anesthesia up to 3 and 3.5 hours. Gachlinger and Poire (*Bull. et mém. de la Soc. de chir. de Paris*, p. 542, 1917).

This is an important hint; as shown by Sajous, ether pneumonia is mainly due to lowering of the temperature in the al-

veoli, the defensive ferments thus losing in part their bactericidal activity, which depends upon the temperature to which they are exposed.—EDITORS.

**Cardiovascular Disease.**—In advanced arteriosclerosis and aneurism ether is relatively contraindicated because of the fact that the rise of blood-pressure it produces may result in rupture of a vessel.

It is difficult to predict how a patient with heart disease will stand an operation. The nature of the lesion counts for far less than the degree of compensation. This applies equally to valvular lesions and to myocardial insufficiencies, though in the latter it is much harder to judge the exact condition. When it is known that a heart lesion exists, the anesthetist usually exercises extreme care, and this appears to be of great benefit to the patient. The use of large quantities of anesthetic within a short time seems to be particularly dangerous. Irregularities of the heart, with one exception, do not appear to be of great importance in giving anesthetics. Extrasystoles usually disappear during the operation and may not return for days afterward. The permanently irregular heart with delirium cordis, however, often causes alarm and the pulse becomes very fast. A. W. Hewlett (*Phys. and Surg.*, Mar., 1910).

The author has had more trouble with operations and anesthetics in septic patients where the heart muscle has been weakened by absorption than in cases of valvular lesions. It is advisable to shorten as much as possible necessary operations upon such septic patients and the minimum amount of anesthetic should be given. Excessive adipose tissue is a distinct contraindication for some operations like the Wertheim operation for the radical removal of cervical cancer. R. Petersen (*Phys. and Surg.*, Mar., 1910).

Any patient with a full, bounding pulse, high blood-pressure and plethoric

appearance, with heavy specific gravity of the urine and excess of uric acid and urates, will, in the absence of heart lesion, take chloroform better than ether. Ingle (Amer. Jour. of Surg., July, 1911).

**Renal Disease.**—The presence of acute renal disorder or of chronic parenchymatous nephritis is a contraindication to ether, which is held to be more irritant to these organs than chloroform on account of the much larger quantity used (in spite of the fact that, volume for volume, chloroform is the more irritating of the two). Ether tends to diminish the quantity of urine, while chloroform tends to cause a marked post-anesthetic increase in the urinary flow. This difference doubtless depends on the difference between the two drugs in their action on the vessels of the splanchnic area, chloroform causing dilatation, while ether tends to constrict. The fact that many renal cases are arteriosclerotic is frequently an additional contraindicating factor with respect to ether.

An extensive research confirmed the decidedly favorable effects of refraining from purgation and reducing the intake of food preliminary to the operation, while at the same time supplying fluids in abundance and warding off anesthesia acidosis by giving glucose and bicarbonate. The vomit after ether anesthesia indicates that there is achylia. The kidneys may show acute damage from the ether; in one fatal case it amounted to intense nephrosis. This may be the explanation of certain tardy fatalities after general anesthesia. K. Gramén (Acta Chir. Scand., Suppl. I, p. 1, 1922).

Albuminuria is caused by ether much oftener than by chloroform, though glycosuria occurs less frequently.

Opinions are by no means unanimous as to the superiority of chlo-

roform over ether in renal cases. In cases with heart weakness, the latter might be preferable.

In nephritis scopolamine-morphine narcosis, nitrous-oxide gas combined with oxygen, or lumbar analgesia should be given preference. Boldt (Med. Record, May 29, 1909).

Atropine reduces markedly ether hyperglycemia; the greatest reduction is in the first 15 minutes. Ross (Jour. of Pharm. and Exper. Therap., Feb., 1919).

**Diabetes Mellitus.**—Both ether and chloroform are contraindicated in this disease, although the use of insulin reduces the risk of coma. Nitrous oxide anesthesia, with or without oxygen, or local anesthesia, is preferable for these cases.

**Anemia.**—Pronounced anemia, *i.e.*, where the hemoglobin percentage is at 50 or below, contraindicates ether.

In operations upon the nose and mouth, ether, as commonly employed, is disadvantageous owing to the necessity of more constant administration of the anesthetic than in the case of chloroform, as well as on account of the greater irritation of the mucous membranes and more profuse flow of mucus and other secretions induced. By the use of intranasal tubes for the introduction of the anesthetic these drawbacks of ether can in part be avoided.

In many intracranial operations, ether is contraindicated because the rise of blood-pressure it causes induces congestion of the local vessels, which, in turn, leads to an annoying amount of hemorrhage.

Patients in whom, upon previous administration of ether, the latter has caused untoward pulmonary or renal symptoms, should not be given this drug at subsequent operations.

**STAGES AND CHARACTERISTIC PHENOMENA OF ETHER NARCOSIS.**—The effects of ether in the course of anesthesia may be divided, from the clinical standpoint, into several stages:

1. The stage of mental confusion or impaired consciousness, in which there is at the start a subjective feeling of general warmth, sometimes a choking sensation, and smarting of the nose and throat. Soon after, the senses of sight and hearing become obtunded, tinnitus may be experienced, and a sensation of stiffness in the limbs may come on. The irritation of the mucous membranes by the anesthetic causes a greatly increased secretion of mucus and saliva. The patient becomes mentally confused, but when spoken to loudly may understand what is said and respond. The pulse is increased in strength and rapidity, and the respiration may be slightly accelerated. Even before consciousness definitely disappears, peripheral sensibility may be lost. There occurs thus a period of "primary anesthesia," during which small operations, such as opening an abscess, may be performed, or the pains of labor in parturient women obviated. The patient may become hilarious soon after the administration of the anesthetic is begun, but the exhilaration usually marks the advent of the second stage.

The author pours 3 to 5 Gm. (1 to 1½ drams) of ether into the cone and, after the patient has taken 10 to 15 deep inhalations, the operation can begin. He terms this method "one-minute anesthesia," since in many cases the operation can be started in about a minute after the first inhalation is taken. He has used the method in about 200 cases. To get

the best results, not only as to safety, but efficiency, the patient must be kept in the narrow zone between the stages of sensibility and excitement. The patient counts after the anesthetic, who occasionally changes the order of the numbers, and the minute the correct answers cease the anesthetic should be stopped and the operation begun. Clifford (West. Med. Rev., Nov., 1904).

The special sense organs become inactive in ether anesthesia long before general consciousness is lost. Vision and audition cease before touch and sense of position. A feeling (anguish or anger, etc.) is the most persistent mental state. In the process of gradual recovery of normal consciousness feeling is first reinstated. Purely intellectual activity, without images, is next in order. Vague tactual sensations, pressure, and sense of position return before sight and hearing. Johnston (Jour. of Abnormal Psych., April-May, 1909).

Many small operations can be performed in the first stage of ether narcosis: It is only necessary to instruct the patient to breathe deeply seven to eight times, and then press a mask saturated with 10 c.c. (2½ drams) of ether firmly upon the face. The anesthesia lasts from five to ten minutes, and is not usually followed by nausea or other after-effects. W. Busse (Therap. d. Gegenwart, May, 1909).

The writer has found it possible to prolong to an hour or more the stage of incomplete anesthesia in which sensibility is abolished, but the patient is still able to respond to questions, give his name, and look around—*Ätherrausch*. He has performed major operations on the leg, abdomen, etc., with this anesthesia, the patients lying quiet, babbling unintelligibly and moving their heads, but otherwise not interfering with the operation. Moszkowicz (Zentralbl. f. Chir., Feb. 5, 1910).

The author has performed 35 **laparotomies** under primary ether anesthesia alone, never letting the patient pass from the stage of "drunkenness"

to that of agitation, and only giving a few drops when there are signs of returning consciousness. Mariani (*Gaz. degli ospedali*, Nov. 15, 1910).

2. The stage of excitement, in which, owing to the probable primary stimulating effect on certain portions of the brain, the patient acts, especially if the ether be given too rapidly, as if he were intoxicated with alcohol, struggling more or less violently and sometimes shouting, laughing, singing, etc. He often tries to remove the gauze or inhaler and to rise from the table. Hallucinations are frequent during this stage, and when ether is administered to a woman, a third party should invariably be present. The heart action in this stage is decidedly accelerated, while the respiration may be irregular, presenting an alternation of complete suspension for a longer or shorter time, owing to reflex inhibition from the irritated respiratory passages, and of compensatory deep and rapid respirations, which tend to bring about sudden introduction of a large amount of the anesthetic. The skin is flushed, warm and moist, the pupils are generally dilated, but the pupillary light reflex, as well as other reflexes, are still present.

3. The stage of completed surgical anesthesia, in which, in addition to entire loss of consciousness, the function of all reflex mechanisms, including those of the spinal cord, is at a standstill. (Since Crile has shown that continued violent stimulation of sensory nerves may produce abnormal changes in the cells of certain centers, the statement that ether anesthesia totally abolishes central activity is no longer warranted.) In

this stage, the muscles are relaxed, the arm dropping when raised. The pulse under ether is still accelerated and of full volume. The respiration is regular, slow, fairly full, and sometimes noisy, in which event the head should be turned laterally in order to cause the uvula to drop to one side and the diameter of the passage to increase. As the period of anesthesia increases, the breathing becomes gradually shallower, and rarely, in long procedures, markedly feeble and once more irregular. The skin in this stage is moist and suffused as before. The pupils are contracted as in normal sleep, and the reflexes, at the beginning of the third stage, disappear in the following order: (1) Patellar. (2) Reflexes of coughing and swallowing. (3) Corneal and conjunctival reflexes. The pupillary light reflex is retained, though the pupil is small. The temperature is slightly lowered—less than with chloroform.

When the ether is stopped at the end of the operation, the patient, in recovering, may pass again through the stage of excitement, though this is regularly milder and shorter than in the beginning. The patient often vomits, probably partly because of the irritation of the pharynx and stomach by the ether, and then falls asleep.

The third stage of ether anesthesia is divided by the writer into 4 strata. One of the most important signs in anesthesia, he states, is the condition of the eyeball. Aside from extraneous circumstances, such as positional asphyxia, hemorrhage, and shock, the patient is safe and in good condition if the eyeball is moving or stationary but eccentric. As he enters the first stratum of the third stage either from above or below, a partial paraly-

sis of the *motores oculi* is manifest, resulting in a rhythmical oscillation of the eyeball, or a stronger tonic contraction of one set than of another, resulting in a stationary but eccentric globe. Occasionally, in alcoholic patients or persons with high reflex tension, a peculiar, slight twitch of the globe, usually in a lateral direction, is noted. This twitch may not occur until from 3 to 5 seconds after the lid has been raised for inspection. When it occurs, either late or early, it means that the paralysis of the *motores oculi* is only partial. If a rhythmical oscillation, an eccentric stationary globe, or a twitching is noted, the patient has not had too much anesthetic and, other things being equal, ideal surgical anesthesia is present. A. E. Guedel (*Amer. Jour. Surg.*, xxxiv, *Anes. Supp.*, 53, 1920).

4. The stage of danger or collapse, where too much ether is administered or the anesthesia excessively prolonged. Here the pulse becomes weaker and more rapid than before, and may not be felt at the wrist. The respiration is shallow, slow and often stertorous, owing to complete relaxation of the muscles of the soft palate; the skin is cold and livid. The pupils are dilated, with the light reflex abolished. The temperature is clearly subnormal. Loss of muscle tone is even more complete than in the stage of surgical anesthesia, and the limbs are in an entirely limp condition. Death, if it occurs, usually results from failure of the respiratory center.

**PREVENTION OF THYMIC DEATH.**—Status lymphaticus, *i.e.*, general hyperplasia of the lymphatic glands, is a familiar cause of death during anesthesia. The thymus is the active factor in the lethal process, when dilated, owing to the pressure it exerts upon the underlying trachea.

Chevalier Jackson by intratracheal examinations *in vivo* showed conclusively that such was the case, the trachea being so compressed in some instances as to prevent the passage of a pin.

Why should ether cause death in such cases? It should be borne in mind that "thymic death," as it is termed, may be caused not only by anesthetics but also the most trivial causes: dancing, running, mental excitement, cohabitation, the mere introduction of a tongue depressor, etc.

Sajous, Sr., answered this question recently (*Anesthesia and Analgesia*, April, 1926) by showing that "just as the secretion of the adrenal medulla regulates the contractile power of the cardiac and vascular unstriated muscle fibers, so does it regulate the contractile power of the unstriated muscle fibers contained in the lymph glands, nodes and vessels." Anesthetics which cause a rise of blood pressure, and excite *primarily* the functions of the adrenals, thus do so not only by the influence on the cardiovascular system, but also by increasing the lymph pressure. The thymus, a lymph gland extremely rich in lymph channels, thus becomes itself, owing to its sponge-like structure, tensely engorged, and if already enlarged, as it is in status lymphaticus subjects, readily becomes sufficiently engorged, tense, and hard as to produce what Sajous has termed "thymasphyxia."

**Treatment.**—The measures indicated to forestall and arrest the lethal trend in such cases are those which empirically have given good results when high blood-pressure is present, as it is likely to be during the stages of mental confusion and excitement.

Here such drugs as strychnine, cocaine, adrenalin, etc., which tend to raise the blood-pressure, would only aggravate the case and perhaps insure death. Conversely, vasodilators, **amyl nitrite**, **nitroglycerin**, **venesection**, and, for the purpose of reducing the viscosity of the blood and lymph and causing general vasodilation, warm **saline solution** injected slowly, are indicated.

#### **METHOD OF ADMINISTRATION.—Preparation of the Patient.—**

Examination of the patient's urine, circulatory system, and if anemia be suspected, of the blood, are prerequisites to a well-conducted anesthesia. The urine should be examined as to amount and for the presence or absence of albumin and casts. Where the amount is subnormal, free administration of water, with or without saline diuretics, is advisable (Hare), while if casts are found in large number, or sugar is present, ether anesthesia is contraindicated.

Where cardiac disease, especially of the valvular variety, is not so marked as already to give rise to pronounced symptoms of insufficient heart function, the administration of some such drug as **strophanthus** has been advised.

In the presence of a hemoglobin percentage lower than 50, ether should be given only in case of great necessity, in view of the destructive action of the drug on the red cells. Some surgeons, however, have placed the danger limit at 40 per cent. The administration of oxygen is of value during and after anesthesia of seriously anemic patients.

Plenty of nutritious and easily digested food should, if possible, be supplied to the patient until the day

before the operation, when the diet should be made light. No solid food or milk should be allowed within several hours of the anesthesia, but water and gruels may be given to within two or three hours of it.

**Glucose** is valuable both before and after operations, not only to prevent or combat acid intoxication, but as a food which makes no call on digestion. A tablespoonful can be given with water and lemon-juice three times or more in the twenty-four hours, or in special cases it may be given by the rectum or intravenously (2.45 per cent). Mortimer (*Lancet*, June 17, 1911).

Mellish advises that **castor oil** be given at least twenty-four hours before the operation, so that the patient will not be depleted of fluids before the intervention. An enema is then given a few hours before the anesthesia. Some surgeons administer only a mild **aperient** some hours before the operation. Others advise against any aperient.

The mouth should always be examined previous to inhalation anesthesia, and such foreign bodies as detachable false teeth, food remnants, chewing gum and tobacco, removed.

Any plate containing artificial teeth should be removed from the patient's mouth if it is so small that if dislodged it might prove dangerous either by being swallowed or lodging in the gullet. Dawbarn (*Jour. Amer. Med. Assoc.*, April 21, 1906).

The writer adds a small amount of **chloroform** to the ether. The mixture is practically as safe as ether alone. It seems safer than chloroform and more rapid in action than pure ether. McCardie (*Brit. Med. Jour.*, Apr. 21, 1917).

It should also be made a rule to wash out the oral cavity with a dilute **potassium permanganate** or **hydrogen dioxide** solution.

The author insists upon the importance of preliminary thorough disinfection of the mouth by inhalations of thymol and by salicylic acid with alcohol and hot water; this is done on the preceding night and just before operation. The antiseptic inhalations are resumed as soon as the operation is completed. This method materially lessens the after-dangers of etherization. Pneumonia induced by etherization is of a different type to the usual form, with lower and less regular temperatures and without the appearance of a true "crisis." The pulmonary signs develop later and there are less cough and sputum. In prophylaxis, stress is laid upon strict limitation of the quantity of anesthetic inhaled and attention to the posture of the patient. A. Otte (Lancet, Dec. 26, 1908).

Any tight clothing over the neck and chest should be loosened before beginning the anesthesia.

The induction had best be conducted in a quiet room. No talking, except to the patient, should be allowed during this period, and no attempt to move the patient should be made in the early stages of the anesthesia. Care should be taken by the anesthetizer to gain his confidence and allay any fears of the anesthesia he may have entertained.

It often happens that only toward the close of an operation is the patient's abdomen in a perfectly satisfactory condition of relaxation from the surgeon's point of view. It is well, therefore, in abdominal cases, to let the anesthetist get to work at the earliest possible moment—as soon, for instance, as the surgeon begins to get his instruments ready. Blumfeld (Lancet, May 31, 1902).

During the first stages of the induction of anesthesia fear may be an important factor in causing a catastrophe. A nervous boy, aged about 9 years, was to have his tonsils and adenoids removed under chloro-

form. He was placed on the table, and a relative was holding his hand. The mask was held before his face, and before any chloroform was poured on it the patient began to breathe rapidly, drumming with his heels on the table, and saying "I'm going." The anesthetist tried to quiet him and told him that he had as yet had no anesthetic, but the rapid breathing continued for a few seconds, and the boy died. Nothing abnormal had been found in the chest before the administration. No *post mortem* was allowed. R. J. Probyn-Williams (Clinical Journal, Dec. 23, 1908).

Moistened gauze or cotton may be placed over the patient's eyes during the administration.

Protection of the eyes in anesthesia is most satisfactorily accomplished by taking small pledgets of absorbent cotton, placing them over the eyes to absorb the tears, and over this a piece of rubber dam large enough to cover both eyes and extend over the eyebrows, with a vent to allow of protrusion of the nose, and which closely adheres to the skin of the face. Over all is placed a flat piece of absorbent cotton of the same shape and size as the rubber dam, with a slit for the nose. This absorbent will catch any drops that may accidentally fall on the face. Samuel Johnston (Can. Pract. and News, Mar., 1912).

Exclusion of two or more extremities from the general circulation during anesthesia has been advised by Klapp and others.

With the application of constricting bands high on the thighs, thus damming off part of the circulating blood, far less of the anesthetic is required. The author first applies a constricting band to collect a certain amount of blood in the legs and then over this applies a tourniquet to shut off the blood as effectually as with an Esmarch bandage. He orders the patient to breathe deeply and tranquilly; the room



should be perfectly still. Then from 10 to 20 c.c. ( $2\frac{1}{2}$  to 5 drams) of ether are given all at once, which is enough for fifteen minutes' anesthesia. For longer operations he gives from 20 to 30 c.c. (5 to  $7\frac{1}{2}$  drams) at once, and then 10 c.c. ( $2\frac{1}{2}$  drams), continuing with the drop method. Klapp (*Therap. Monats.*, Jan., 1910).

Klapp's method applied. Six patients developed thrombosis among the 75 laparotomized. None of the patients was subject to varicose veins. The thrombosis in the leg in each case was transient and harmless, but it has convinced the author that this method has too many dangers. The thrombosis developed exclusively after laparotomies, nothing of the kind having been observed after 110 vaginal operations. Gräfenberg (*Deut. med. Woch.*, Feb. 3, 1910).

Klapp's method used in 71 cases. Thrombophlebitis developed in 3 cases. With part of the circulation shut off the tendency to vomiting ceased to be materially reduced, but this advantage was counterbalanced by the sense of weight and tingling in the legs in the first few days after the operation. In the 3 cases in which thrombophlebitis developed the constriction had been applied for from sixty to seventy-two minutes; the operations were for hernia or ankylosis of the knee. Donati (*Riforma medica*, March 14, 1910).

Report of 63 cases in which an Es-march bandage was applied to the legs or arms or both to exclude these members from the general circulation. The amount of chloroform necessary for major operations thereafter was much lessened. The first phase of anesthesia was shortened, the nerve-centers feeling the effect of the anesthetic remarkably early, and the patients rousing afterward much quicker. No by-effects were observed. Berri (*Gaz. degli ospedali*, May 22, 1910).

Upon contracting the circulation during general anesthesia by applying tourniquets to the extremities, there is less bleeding in operations on the head, neck, and trunk, and even on a non-

obstructed part of an extremity. The method may be applied for hemorrhages occurring during childbirth and internal hemorrhages. The author applies the small rubber tube near the axilla and groin under slight tension before beginning the anesthetic. He withholds the chloroform until there is a bluish-red congestion of the extremities. The veins are almost completely obstructed by the tourniquet and the arteries only partially, the back pressure completing the blockage in them. Hans (*Zentralbl. f. Chir.*, Bd. xxxvii, S. 1579, 1910).

Klapp's technique employed in 1144 cases, using chloroform, and in 35 with ether. When the constriction was removed, the blood and tissues excluded from contact with the anesthetic diluted and took it up rapidly. The patient roused at once or in about ten minutes, and the postanesthetic disturbances were reduced in frequency and intensity. In case of accident, removing one or more of the bands flushes the system with fresh blood and starts up the respiration anew. The members feel a little numb or there may be minute ecchymoses. Postoperative phlebitis developed in 4 cases. Heart and vascular disease or general infections may contraindicate the method in certain cases, but it has special advantages in all cases of kidney and liver disease. Delagènière (*Bull. de l'Acad. de Méd.*, July 25, 1911).

**Posture.**—The patient's head may either rest on the table or be somewhat elevated by a firm pillow, in order, as much as possible, to remove tension from the anterior tissues of the neck and facilitate breathing. Where there is pus on one side of the thorax the patient should always be turned upon that side during anesthesia, in order that the opposite lung may be wholly unhampered in its work, as well as to prevent any pus from entering the bronchus of the sound side (Probyn-Williams).

Stress laid on comparative frequency of paralyses of the brachial

plexus after operations in Trendelenburg's posture which, the author believes, are due to pressure exerted on the plexus at a point between the clavicle and the first rib. In addition he has noted minor disturbances such as temporary numbness, crawling sensations, etc. All these unpleasant phenomena can be avoided by arranging the arms in a proper manner and at the same time noting the amount of compression to which the arteries are subjected. The pulse at the wrist is a valuable guide. The arms should be fastened to the sides, below the table, with a cushion under each arm. Rothe (*Zentralbl. f. Gynäk.*, Nu. 12, 1904).

The author recommends, in vaginal operations, placing the arms across the chest and keeping them in position by winding the lower part of the sheet under them. In laparotomies, the arms are crossed under the back. In this manner, they are kept from hanging over the edge of the table with the possible result of a pressure paralysis. Preschnig (*Zentralbl. f. Gynäk.*, June 25, 1904).

Patients with any pre-existing respiratory affection should not, as a rule, be placed in the Trendelenburg posture. F. W. Hewitt (*Lancet*, Aug. 10, 1907).

While a patient is in the Trendelenburg position the percentage of decrease in the excretion of urine is 58 per cent. in ether anesthesia and 82 per cent. in anesthesia by chloroform. This great decrease is not, even in moderate degree, due to urine being retained in the renal pelvis, nor to unsatisfactory drainage by the catheter. In renal inefficiency and cardiac and arterial lesions it seems that the use of the Trendelenburg position introduces a special element of danger, and this less markedly when ether is used than when chloroform is employed. Bovée (*Amer. Jour. Med. Sci.*, Jan., 1911).

In operating upon the nose and throat the two main reasons for desiring the upright position are:

First, that more skillful and therefore more satisfactory work can be done when one can make use of the same topographical relationship with the patient as that to which one is accustomed in every-day office practice. Second, that in any operative work about the head less blood is lost when the patient is upright. In routine operations performed in the nose and throat, even without alertness in sponging, embarrassment from blood flowing into the windpipe does not occur.

The elevation of the body from the recumbent to the upright position should be made slowly. The secret of a safe and uninterrupted administration of an anesthetic in the upright position is in keeping the neck somewhat stretched and the head moderately extended over the head-rest. T. R. French (*N. Y. Med. Jour.*, Mar. 16, 1912).

**Preliminary Medication.—Morphine sulphate**,  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.008 to 0.016 Gm.), and **scopolamine hydrobromide**,  $\frac{1}{200}$  to  $\frac{1}{100}$  grain (0.00032 to 0.00065 Gm.), are not infrequently given hypodermically in a single or in divided doses in the two hours preceding anesthesia. The combination acts as a decided adjuvant to the action of the ether, reduces the amount of the latter to be administered, places the patient in a drowsy state previous to operation, and tends to prevent excitement during the induction. Its disadvantages are, that it renders observation of the pupil practically valueless in judging of the depth of anesthesia, and that the patient remaining narcotized some five or six hours after the end of the operation, constant watching is necessary during this entire period. The method should not be used in cases of heart disease, and must be employed only with caution in aged persons as well as in the young.

**Scopolamine and morphine** used in 132 cases before ether was administered. In only 2 cases did the writer observe initial excitation of the patient. In 102 cases the average period of induction was eleven minutes. The excitement stage is practically eliminated. Vomiting during operation is rarely seen. There is no secretion of mucus and the respirations are as noiseless as in chloroform anesthesia. The respiration is considerably checked and, consequently, dehydration of the body is diminished. The amount of anesthetic is markedly reduced. In 131 cases the average amount of ether per hour was exactly 4 ounces (120 c.c.). The patient usually sleeps a considerable time after the operation and is thus relieved of the initial pain and vomiting. Forty-two per cent. had no post-operative vomiting. The anesthetic may be withdrawn for considerable periods during the operation and almost always after the closure of the peritoneum. In 1 case (a vaginal hysterectomy) it was withdrawn for fifty-five minutes. In another (the removal of a large cyst) the patient went fifty minutes without ether. In none of the cases was there pneumonia or bronchitis. The scopolamine-morphine mixture is of much advantage in nervous women undergoing abdominal or pelvic operations and in whom there is no contraindication. R. Mauritis (Physician and Surgeon, Mar., 1910).

The authors have used **hyoscine** and **morphine** in over 200 cases as a preliminary to general anesthesia in adults. The ordinary dose was hyoscine  $\frac{1}{400}$  grain (0.0006 Gm.), morphine  $\frac{1}{6}$  grain (0.01 Gm.), atropine  $\frac{1}{180}$  grain (0.00035 Gm.), hypodermically, one to three hours before operation. In young women the dose of hyoscine was sometimes  $\frac{1}{200}$  grain (0.0003 Gm.). The majority of patients had the previous night 10 grains (0.6 Gm.) each of **trional** and **sulphonal**. Fifteen minutes after the hypodermic injection the patient is completely indifferent to his sur-

roundings. He walks into the operation room (when his condition permits) without apprehension, is somewhat dazed, but replies intelligently to questions, usually takes the anesthetic without terror or struggling, and when he wakes up some hours later remembers nothing that has happened. Less of the anesthetic is required, the quieting effect on alcoholic is noteworthy, and post-operative vomiting is much less frequent. In no case were there ill effects. In cardiac cases the procedure adds an element of safety. The authors have not carried it out where there has been albuminuria. Darling and Williamson (Dublin Jour. of Med. Sci., July, 1911).

In cases of **goiter** and glandular growths pressing upon or displacing the trachea, the safest method, if ether is used, is to inject **atropine** gr.  $\frac{1}{100}$  (0.0006 Gm.), or this together with **morphine** and **scopolamine**, half an hour before giving ether by the open method. In this way a certain diminution of the bronchial secretion can in some cases be obtained. In large numbers of cases of goiter, both simple, malignant, and exophthalmic, the author has used chloroform in low percentage vapor with a copious stream of **oxygen**. This plan has answered extremely well, and possesses the great advantage that one can readily lighten and deepen narcosis as the steps of the operation demand. Buxton (Brit. Med. Jour., Nov. 4, 1911).

All patients, except possibly those under 8 or over 80, should have preliminary medication. It is much easier to anesthetize a patient half-asleep than one with the reflexes all in rebellion. The tissues of the human body, after an operation lasting an hour or more, are in a condition that, if evil effects are to follow the use of ether or chloroform, they are apt to occur. Here **nitrous oxide** and **oxygen** should be introduced cautiously and quietly. The patient should be under the gas less than two minutes. The author does

not believe in the drop method as a constant one. He uses it daily at some time in the anesthesia, but considers the vapor method with warm, attenuated, moist air its superior by far, and superior to the nitrous-oxide and oxygen method. At the close of every operation the patient should have from 1 to 2 pints (500 to 1000 c.c.) of warm **saline** with 1 ounce of **glucose** per rectum to relieve thirst and fill out the veins. As the operation is closing or a little later, an **enema** of 3 to 6 ounces (90 to 180 c.c.) of warm **olive oil** should be given to restore the opsonic index. With these precautions, not 1 patient in 10 will have any nausea, vomiting, or unpleasant recollections of the operation. J. C. Gwathmey (Jour. Amer. Med. Assoc., Feb. 17, 1912).

**Essential Oils.**—Their use has been recommended to facilitate the induction of ether anesthesia. As far back as 1902, Briggs advised that 1 dram (4 c.c.) of the **oil of peppermint** or of a 50 per cent. solution of **menthol** in alcohol be sprinkled over the inhaler and respired by the patient for about three minutes before the administration of ether was begun. More recently Gwathmey has recommended the preliminary administration of **oil of orange**. The value of these oils, which recent experience seems to have confirmed, consists in rendering the induction more easy and rapid and the anesthesia "smoother" throughout, in overcoming all tendency to coughing and choking sensations, in suppressing or greatly shortening the period of excitement, and in diminishing the post-anesthetic vomiting.

The **essence of orange-ether method** overcomes, according to the writer, the usual objections to a closed method. It has been used in 1000 cases without a fatality of any kind. It furnishes a volume of air sufficient

for respiration with an amount of anesthetic sufficient to produce anesthesia. Rebreathing of small quantities of  $\text{CO}_2$  is a means of maintaining cardiac and respiratory function and preventing shock. The patient leaves the table in good condition, and recovery is shorter than by any other method of ether narcosis. There is an absence of prolonged nausea and vomiting. The vapor is constant in strength, moisture and warmth. Ether waste is eliminated. The average time required to get surgical anesthesia is 6 minutes. This method approaches the ideal more closely than other methods on account of the rapid, pleasant induction, devoid of excitement; the even maintenance, under perfect control, with perfect relaxation; the air supply sufficient for oxygenation with partial rebreathing, and the prompt and uneventful recovery. I. D. Kruskal (Trans. Amer. Assoc. of Anes.; Jour. Amer. Med. Assoc., Aug. 5, 1916).

Mellish was able to corroborate the statements of Briggs concerning the efficiency of **peppermint oil** in the same directions.

**Ether-Oil Anesthesia by the Rectum.**—This method of producing anesthesia was introduced by James T. Gwathmey, of New York. The apparatus required is very simple: an india rubber catheter, a funnel, a medicine measure, an empty medicine bottle with a cork for shaking the mixture; this shaking must be done forcibly for 2 minutes.

Gwathmey (1920) attributed the following advantages to colonic anesthesia after an experience of several years: (1) It was one of the easiest methods to administer, requiring only a rectal tube with funnel attached and quiet surroundings for the patient. (2) It was one of the safest methods, the margin between full surgical anesthesia and a

toxic dose being greater than with any other method. (3) It was one of the most pleasant methods for the patient, as attested by the fact that those who had tried other methods preferred the colonic. (4) It resulted in a greater relaxation of the musculature than was usual with any inhalation anesthetic. (5) It required a smaller amount of ether per hour than any other method of administering ether, the estimated amount being 2 ounces (60 c.c.) per hour, which seldom varied. (6) It was regulated as easily as any inhalation method; by covering the face with a towel to deepen the anesthesia, by placing an airway tube to lighten, or by unclamping the rectal tube and draining the residue and flushing thoroughly, it could be terminated at any time so far as the anesthetic was concerned, the patient continuing to sleep from the other drugs used. (7) The brain was more completely protected against reflex stimuli than by any other method of inhalation anesthesia, as proved by the fact that the patient at times changed his position or conversed with the surgeon, as in spinal analgesia.

As carried out satisfactorily by H. M. Page and G. B. M. White (Lancet, Oct. 27, 1917), a simple cleansing of the bowel an hour or 2 before the injection in addition to the usual dose of medicine is an advantage. One-fourth of a grain (0.016 Gm.) of **morphia**, and  $\frac{1}{100}$  grain (0.00065 Gm.) of **atropine** is given half an hour before the **ether-oil** injection. From 20 to 25 minutes before the time of operation 6 ounces (180 c.c.) of a mixture of 2 parts of ether and 1 part of oil are slowly administered by the rectum, 6 minutes being spent in making this injection; the catheter is passed 3 or 4 inches into the rectum. When the operation is finished the remaining **ether-oil** must be washed out, using a

large rectal tube and funnel. The washing is continued until no ether or oil can be detected in the returning fluid. Before withdrawing the tube 3 ounces (90 c.c.) of **olive oil** are passed into the rectum and left there.

By following this technique there have been no rectal, pulmonary, nor gastric sequelae. Return of consciousness is not delayed when washing out is done well.

The dose of ether for rectal anesthesia depends upon the age and weight of the patient, about 1 ounce (30 c.c.) of ether being required for each 25 pounds of body weight. This may be lessened when paraldehyde is used. More than 6 ounces (180 c.c.) of a 75 per cent. oil-ether mixture should not be given to adults, regardless of weight. The ocular reflexes should never be abolished, and stertorous breathing should not be allowed to continue. W. M. Johnson (N. Y. Med. Jour., Oct. 28, 1916).

The writer regards rectal ether-oil anesthesia as a very valuable method, provided the proper technique can be obtained and a suitable dose given. He regards it as being as safe as or even safer than the usual inhalation methods, and believes it to be applicable to all cases from 3 years upward, and of especial value in all operations about the head and neck. He suggests rehearsing for a week or more before operation every detail of the technique of administration, since in this way the element of fear can be almost if not entirely eliminated. H. W. Sweetnam (Med. Jour. Austral., 1, 452, 1918).

The writer has a record of 160 operations on the ear, nose or throat of children from 1 to 12 years old, under ether anesthesia by the rectum. This experience has convinced him that this procedure is absolutely harmless for children. They are less susceptible than adults to the possible actions of ether, either from absorption or by reflex action from the intestines. If the ether is eliminated by the lungs too rapidly, respiration can be hindered and thus the action of the anesthetic prolonged, or a few whiffs

of **chloroform** can be given in addition. There is no phase of excitement with ether given by the rectum, but there may be a tendency to vomit and hence the stomach should be empty when the child comes to the table. Vomiting with the ether alone does not occur till tardily, usually the next day. Ilinojar (Archivos Españoles de Pediat., Nov., 1918).

The writer reports 120 operations on children done under rectal anesthesia, and comments on the ease and facility of the method, especially in operations on the head. The ages ranged from 2, 4 and 5 months to 16 years. There were 7 deaths, but the anesthesia could not possibly have been

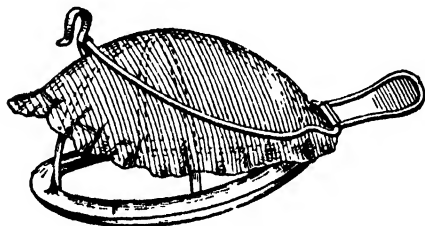


Fig. 1.—Schtimmelbusch's mask.

incriminated in 5, and in the 2 others any connection with the anesthesia seems highly improbable. De Souza (Arch. de Méd. des Enfants, Dec., 1920).

In a further communication the writer states that colonic ether anesthesia is automatically maintained by the ether separating from the oil according to certain inflexible physical laws. It is impossible to have deep anesthesia at one time and light anesthesia at another, unless the anesthesia is deepened by rebreathing or lightened by an airway tube. There is no irritation of the lungs, and mucus and saliva are usually absent. The temperature of the patient remains normal. The skin is warm to the touch; the color of the face suggests thorough oxidation all the time, and quiet respiration, normal pulse, and good color indicates that no toxic condition exists. There is absence of nausea and vomiting. The writer proposes to take advantage of

the principle of synergism and to convert colonic anesthesia into **synergistic colonic analgesia**. **Magnesium sulphate** (6 to 15 c.c.— $\frac{1}{16}$  to  $\frac{1}{2}$  ounce), given by hypodermic injection 2 hours before operation, followed by **morphine sulphate** hypodermically (from  $\frac{1}{12}$  to  $\frac{3}{4}$  grain—0.005 to 0.024 Gm.) one hour before the operation, when supplemented by **nitrous oxide** and **oxygen** (the oxygen being employed in a much higher percentage than usual), gives a safer and better relaxation than when ether is used. J. T. Gwathmey (Jour. Amer. Med. Assoc., Jan. 22, 1921).

**Administration and Dose.**—The apparatus used in general ether anesthesia ranges from the simple to the decidedly complex. The "*open method*," reduced to its simplest expression, consists merely in the placing of a number of thicknesses (8 to 12) of gauze over the patient's mouth and nose, and dropping ether in gradually increasing, then constant amount upon the gauze. A method formerly much, but now less, employed, consists in the use of a cone or cornucopia made with a towel supported by felt or pasteboard, the base of which rests over the face, and at the apex of which an opening is provided, which is filled with gauze, upon which the ether is dropped.

There is a tendency to the excessive administration of ether and insufficient entrance of air with this method, which has led to the general adoption of different procedures.

Recommendation of the use of a cone about the size of a quart tomato-can, with ends removed and sides flattened enough to give an oval shape. The top of the cone is closed by laying several layers of gauze over it, and onto this gauze the ether vapor traverses 5 or 6 inches

of warm air space, and reaches the mouth and nostrils of the patient, it has been pretty thoroughly mixed with air and is warm.

The gauze roof of the chamber offers sufficient obstruction to the expired air so that at the beginning of inspiration the air chamber is full of expired air. The rebreathing aids in conserving the normal amount of carbon dioxide in the lungs and, therefore, in diminishing the danger of acapnia and shock. If the anesthetist wishes to concentrate the ether vapor, additional layers of gauze, permitting the use of more ether, may be employed or the cone may quite easily

such as colitis, hemorrhoids, ulcers, fistula and in emergency cases. Its advantages are the prevention of shock, narcosis of smooth and uniform depth, and nearly normal pulse and respiration. There is little or no change in blood-pressure; the reflexes are not disturbed; hypersecretion of mucus is absent; there is less hemorrhage in mouth, head and neck surgery.

Nitrous oxide and oxygen anesthesia he considers the luxury of all inhalation anesthetics. It has proved to be 100 per cent. efficient for any operation. J. A. Zabrocki (Dental Cosmos, lxx, 993, 1917)

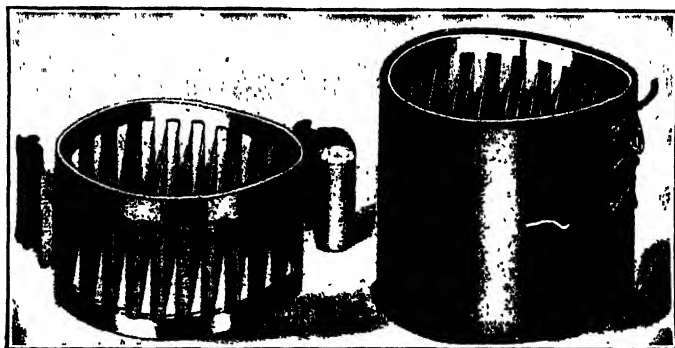


Fig. 2.—Allis's ether inhaler (Fowler). Showing fenestrated metallic frame with a muslin roller in course of application, and the inhaler complete with cover.

be closed, partially or completely, by a towel applied over the gauze top. C. P. Bull, Jr (Med. Record, May 24, 1913).

The open drop ether method is a crude and unscientific method, and is responsible for all the ill-repute that ether bears as regards nausea and vomiting. It is irregular and uneven, and predisposes to acidosis. The nitrous oxide-ether method is dangerous; it tends to raise the blood-pressure enormously, to make the patient cyanotic, and is responsible for many deaths. The writer advocates **oil-ether** anesthesia for neurotics and in all operations upon the respiratory tract, head, neck, mouth, jaws, chest, tonsils and for goiter and adenoids. It is contra-indicated in all pathological conditions of the lower bowel,

One of the plans now often followed involves the use of a wire frame or mask, such as that devised by Schimmelbusch (see Fig. 1), which is laid over the patient's face and covered with several layers of gauze. A piece of gauze tissue or other absorbent material, with an opening in the center which is placed over the mouth and nose, may with advantage be used beneath the mask, *i.e.*, in contact with the skin. The evaporating surface has to be larger for ether than for chloroform, and at least twice the number of layers of gauze is required for the former anesthetic.

Ether is given by the drop method through a mask covered with gauze,

slowly at first, and as soon as the patient becomes accustomed to the vapor the quilted cover is fitted over the mask, with the base carefully approximated to the patient's face, and the drug is then dropped onto the gauze through the aperture. By this method patients are put under and kept under the anesthetic with a minimum amount of drug. Pearson (Jour. Amer. Med. Assoc., Nov. 23, 1912).

An apparatus is described by the writer for administering oxygen in combination with ether, chloroform, or both. An oxygen cylinder is connected with a 3-bottle apparatus. Valves control the passage of oxygen through the bottles, which contain respectively chloroform, ether, and water. Employment of this method in nearly 1100 cases indicated its simplicity, economy, absence of cyanosis, and infrequency of post-anesthetic vomiting. H. R. Phillips (Proc. Roy. Soc. Med., xi, Sect. Anesth., 13, 1917).

A double mask for ether narcosis is recommended by the writer. The inside mask, which is covered with gauze, has a second much higher mask fitting tightly over it, which is likewise covered with gauze. On the second mask, the gauze is held in place by a metal ring with a spring. At the highest point of the outside mask an opening is made in the gauze, and either a small funnel is introduced to carry the anesthetic to the mask below, or the ether is poured a drop at a time directly on the inside mask. The amount of ether required is thus reduced one half, as the fumes do not evaporate so quickly in the enclosed space. No disagreeable features have been observed. Jatrou and Wessely (Zeit. f. Chir., Jan. 27, 1923).

A still more perfect and widely used instrument is the Allis inhaler (see Fig. 2), provided with perpendicular, parallel linen partitions which allow a free passage of air to the patient, while also providing ample surface upon which to drop and vaporize the ether.

The author uses the Allis inhaler. Just before beginning he places 3 pieces of sterile gauze on it, and in 2000 cases has had no pneumonia. The cone should be placed on the face with the head a little elevated so as to sit at an angle. The eyes are covered with a folded towel.

He starts with 1 drop of ether, then in a second adds 1 more drop, then 2 drops, 4, 10, up to 30, and continues the 30-drop doses until anesthesia is complete, when a few drops every few seconds will keep a patient under. G. Spencer (Amer. Med., July 11, 1903).

There are but few occasions in which ether may not be given to children in preference to other anesthetics. The most important of these are conditions such as acute bronchitis, pulmonary congestion or pneumonia. The open method should be adopted always. The smaller size of Allis's inhaler should be used. This should have a clean, folded towel pinned closely about it, and permitted to extend about an inch below the lower margin of the cone. The open end of the cone should always be allowed to remain free and unmolested. If the child is very much reduced from prolonged disease, and the operation is apt to be a long and dangerous one, the child's body should be swathed in cotton-batting or an electrotherm used. Elmer (Arch. of Pediatrics, June, 1905).

The mask used by the author is of the Allis type and dimensions, improvised from sulphite fiber covered with zinc oxide plaster, and has the Allis face-piece of rubber and a floor of wire on which are placed some layers of gauze. Within the mask is placed a 16 candle-power incandescent globe covered with several layers of gauze. The top of the mask is covered with dentist's rubber-dam tissue, in which is cut an opening about the size of a silver quarter. The anesthesia is begun with chloroform. The current is turned on with the mask about three inches from the patient's face. The drop method is used and continued until the patient acknowledges sleepi-



ness, which is usually in from three to five minutes; then ether is substituted for the chloroform. The ether can is merely punctured with the point of a needle and the ether is forced out by the heat of the hand and sprayed on the gauze over the light, whose heat so rapidly volatilizes the ether that, in from three to seven minutes more, operative anesthesia is secured without any struggling, sense of suffocation or hypersecretion. The advantages of the method are: (1) lessened amount of anesthetic; (2) absence of the danger of ether pneumonia due to the chilling of the lung tissue; (3) absence of kidney complications because of the very small quantity of anesthetic to be eliminated; (4) almost total absence of post-operative nausea and vomiting. McRoberts (N. W. Lancet, Aug. 15, 1909).

The pallor and syncope of a too open method of giving ether are due to acapnia, while by a closed method with a fair amount of rebreathing an excessive loss of carbon dioxide is prevented, visceral tonus is maintained and the circulation kept good, as shown by the pink color of the skin. The Rovsing mask and bag afford a good method of controlling the rebreathing. By observing the color of the skin one can judge the condition of the circulation. The anesthetist should keep the color a wholesome pink. Bryant and Henderson (Jour. Amer. Med. Assoc., July 3, 1915).

After a small quantity of ether has been poured upon the gauze, it or the mask covered by it should be held at first some distance above the patient's face, and only gradually brought in contact. Ether vapor, being heavier than air, tends rapidly to sink into the patient's nose and mouth and by its irritating properties is therefore likely to cause, especially at first, gagging, respiratory arrest and marked subjective discomfort. By gradual ap-

proach of the mask to the face, time is allowed for the mucous membranes to become accustomed to and partly anesthetized by the vapor, whence the irritation is no longer felt and discomfort ceases. After this tolerance has become established the agent may be pushed somewhat more rapidly, though it is only occasionally advisable to make the ether vapor more concentrated than the average required to induce anesthesia in the customary period of ten or twelve minutes, as any excess over this concentration is likely to harm the mucous membranes and predispose to subsequent complications. To attempt to accelerate anesthesia by limiting the supply of air is a still more unwise procedure.

Following plan advised for the administration of ether: The ordinary Esmarch or chloroform mask, covered with six or eight layers of gauze, is held three or four inches above the patient's mouth and nose. The patient is directed to count slowly after the anesthetist, or to breathe in and out, or to blow the vapors away. The ether contained in the ordinary chloroform bottle with dropper is allowed to drop on the mask somewhat more rapidly than if it were chloroform. The bottle is moved continuously, so that each drop falls on a different spot on the mask, and is freely mixed with air.

The mask is lowered gradually; at the same time the drops of ether are increased until a very fine, continuous, steady stream is being spread over the entire mask. The mask is finally lowered until it almost touches the face. The average patient will be able to count from 70 to 80, some only 40 or 50, while others may count 120 before unconsciousness begins. This will require from two to three minutes. At the end of a period of from five to seven minutes the patient relaxes and becomes sufficiently

unconscious so that the final preparations for the operation may be begun. By the time these are completed the patient is in a condition of surgical anesthesia. To accomplish this from 2 to 2½ ounces of ether have been administered, and from twelve to fifteen minutes have elapsed. Less ether is then given. Metzenbaum (*Jour. Amer. Med. Assoc.*, Nov. 17, 1906).

In the treatment of accidents most dependence may be placed upon inhalations of **ammonia** and **oxygen**. H. L. Springer (*N. Y. Med. Jour.*, June 13, 1908).

When employing the open method, the authors place a ring-shaped pad around the nose and mouth of the patient, and upon this place the inhaler. Thus the patient cannot inspire or expire air laterally. Hewitt and Symes (*Lancet*, Jan. 27, 1912).

Patients should not be moved after the anesthetic has been started. Short-necked persons breathe better when the head and shoulders are on a plane higher than the abdomen.

A few drops of a 25 per cent. solution of **oil of bitter orange** in alcohol sprinkled on the mask is of benefit, especially in children.

Restricted or imperfect breathing may be due to nose breathing, too strong a vapor, or fear of the patient to breathe. Encouragement, reassurance and patience usually overcome this. If this breathing persists after consciousness has been abolished, rubbing the lips briskly with gauze or the finger tips or sponging out the pharynx will restore the respiratory rhythm. Those with edentulous or pendulous lips may give trouble in the second stage, the lips being sucked in during inspiration, allowing little air or ether vapor to enter. This can be remedied by a dental prop or gag. When morphine has been given and shallow breathing occurs, the anesthetic must not be crowded; a few drops of **aromatic spirits of ammonia** on the mask or **lip friction** often corrects this. In heavy smokers the anesthetic vapor may excite cough, retching or vomit-

ing. This can be helped by allowing the patient to count aloud or placing him on his side.

There are two important reasons for lessening or controlling the excitement and intoxication phenomena during incipient anesthesia: (1) The danger of too much ether vapor inhalation, and (2) the muscular spasm which may introduce an asphyxiating factor. These can be eliminated by care and patience, although in some cases, usually in alcoholics, tobacco and drug addicts, difficulties will arise. To secure complete muscular relaxation, it is best to give some preliminary narcotic and induce anesthesia slowly and evenly. Where this is difficult to accomplish, raising the patient's head and shoulders at one end of the table and his pelvis at the other should be tried. D. E. Hoag (*Colorado Med.*, xv, 223, 1918).

The "drop method" of administering anesthetics, introduced by Witzel, consists essentially in placing the ether or chloroform on the mask in a steady, periodic, drip rather than in larger amounts at longer intervals, and also in carefully adjusting the dosage—*i.e.*, the frequency of the drops—to the conditions present at each moment of the anesthesia. The term is often applied indiscriminately to the "open method" in general, and is conducted, at least in the beginning, with the simple means already referred to, *viz.*, a mask covered with gauze, or gauze alone. J. W. Kennedy carries out the ether "drop" procedure with a gauze towel, one yard square, which is folded into a pad nine inches square and placed in the form of a tent over the patient's face. The thumb and index-finger control the gauze, while the rest of the hand splints the lower jaw to the upper. After allowing the patient a few breaths of air, the anes-

thetist begins dropping the ether, and continues to drop it without intermission until surgical anesthesia is reached. If the induction is properly carried out, according to Kennedy, there is no stage of excitement and anesthesia is rapid. Where the patient coughs or struggles in the first stage, the quantity of ether should be temporarily diminished, but if the excitement characteristic of the second stage appears, the anesthetic should be dropped on more rapidly. S. G. Davis, who uses an inhaler covered with only 6 layers of gauze, advises that about the time when the patient will no longer respond to questions, a moist towel or some additional gauze be wrapped snugly around the base of the mask. The patient becomes unconscious in two or three minutes and is ready for operation in about ten minutes.

The author administered ether 337 times by the open drop method. The average time of inducing anesthesia was six minutes and ten seconds. The time varied from forty seconds to twelve minutes. Initial vomiting did not occur in a single case. In 65 per cent of the cases there was no struggling or choking; in the remaining 35 per cent. excitement and choking occurred in a mild degree. No patient needed stimulation. Forty-eight per cent. had no nausea or vomiting following the administration; 40 per cent. were slightly nauseated. There was no postoperative pneumonia in any case. Nephritis occurred in the case of 3 patients; 1 was a woman suffering from melancholia, which developed during pregnancy; the second was a patient suffering from appendicitis of ten weeks' standing; the third was a woman with a large uterine fibromyoma. In all 3 the physical condition was extremely poor. Shipp (*Lancet*, April 14, 1906).

The author describes a modified method of drop etherization. A square

pad of gauze twelve layers thick, large enough to cover the patient's mouth and nose, extending well down over his cheeks, is laid directly on the patient's face. Ether is then dropped on by means of an ordinary bottle with a small wick inserted through a slit in the cork. Ether having been dropped slowly for about one minute on the pad of gauze described above, another similar pad is laid on, and the rapidity of the drops is increased and continued until the patient becomes thoroughly anesthetized. It is very important that the ether be gradually administered. The method is less disagreeable to the patient and does not cause suffocation. Postoperative vomiting is reduced from nearly 100 to 32.5 per cent. There is quicker recovery of consciousness, and there is reduction of postoperative acetoneuria from 88.5 to 26 per cent. Ladd and Osgood (*Annals of Surg.*, Sept., 1907).

For dropping ether the author suggests cutting through the soft metal cap of the ether can about four-fifths round, so that the cap can be bent back without fracture. A small pledget of absorbent cotton shaped to a wick is then inserted, and the flap turned down on it, thus forming a dropper. After use, the flap can be turned back and a cork inserted in the can. Lumbard (*Med. Record*, Oct. 24, 1908).

The open or drop method permits of normal oxygenation and avoids contamination of the inspired air, affords a fairly uniform ether vapor with very little distress to the patient, favors muscular relaxation, avoids exaggerated abdominal breathing, is simpler for the inexperienced anesthetist, and its safety has been demonstrated by extensive usage. On the other hand, it produces great refrigeration, gives an incomplete diffusion of ether vapor and air, requires large amounts of ether, and is slower in inducing anesthesia. The semiopen method is such as to permit of a limited amount of rebreathing. It is attained by the use of extra layers of gauze or gauze surrounded by towels, by the use of a cone containing gauze, but with both ends open, or

by any one of the several inhalers arranged for limiting the air supply. Cunningham and Anderson (*Jour. Amer. Med. Assoc.*, Nov. 7, 1908).

Experiments upon lower animals with the different methods of giving ether. Ether administered with an atmosphere of oxygen caused bronchial symptoms and some bronchorrhea, which, however, rapidly disappeared. The drop method produced slight changes in the bronchial epithelium and parenchyma of the lungs, but the alveolar epithelium was unchanged. The damaged epithelium recovered in a few days. When dangerous after-effects are produced they are due to the use of too concentrated vapor. Offergeld (*Lancet*, Dec. 26, 1908).

**Tonsil and adenoid operations** in children and young persons under 18 should practically always be done under a general anesthetic; over that age, when the patient has sufficient self-control and can co-operate, the author prefers local anesthesia with cocaine. The best method of giving ether or chloroform is the "drop method" on gauze, except in patients who require prolongation of the anesthesia, when the author has the anesthesiologist change to the vapor method, passing the ether through warm water in a wash bottle by means of a bulb compression apparatus. He always operates with the patient in the dorsal decubitus, with the head somewhat dropped over the end of the table. The upright position adds greatly to the danger of ether and chloroform. As for the anesthetic, the author decidedly prefers ether. F. R. Packard (*Jour. Amer. Med. Assoc.*, Aug. 28, 1909).

Ether by the drop method may be given to a patient at any age. The author has administered it successfully to a patient 3 days old, and to one of 98 years. Samuel Johnston (*Can. Pract. and News*, March, 1912).

An effective method for dropping ether in emergency is suggested by the writer. Any screw cork, if screwed down tightly will seal the

bottle. By loosening the screw cap 1 or 2 turns it may be regulated to drop as slowly or rapidly as desired. Catherine Patterson (*N. Y. Med. Jour.*, Mar. 30, 1918).

The signs indicating that the patient is ready for operation include contraction and immobility of the pupils, relaxation of the muscles of the jaw, and abolition of the corneal reflex.

The best way to determine if the patient is sufficiently anesthetized is by raising an arm and determining whether it is still rigid or not. The author does not believe in using the eyes as a test at this stage of the anesthetization, for if the patient is resting quietly, but still not yet completely under the influence of the ether, it is likely to excite resistance.

When the patient interrupts the deep natural breathing with a heavy sigh, this is a positive sign that more ether is needed. H. S. Wieder (*Therap. Gaz.*, Dec., 1907).

When the anesthesia is deep enough to suspend the swallowing reaction to salivation, the right moment is at hand for the operation to begin. J. Landström (*Zentralbl. f. Chir.*, Oct. 30, 1909).

The true test of what may be called artistic anesthetizing is to be found in the rapidity with which the patients regain semi-consciousness after the operation. If the anesthesiologist is able to detect and maintain, even for a lengthy administration, an almost indistinguishable degree of lid-closure when the cornea is lightly touched, this speedy recovery will take place. F. W. Hewitt (*Lancet*, March 5, 1910).

The muscles of the jaw seem to feel the effect of the anesthetic before any others. The cessation of the contraction in the masseter is a much more reliable index than the sensory signs and changes in the reflexes, as this relaxation indicates that the muscles in the field of operation are likewise relaxing, which is not always the case

when only the reflexes are abolished. Fiori (Policlinico, March 13, 1910).

The "*closed method*" of inducing anesthesia involves nowadays the use of more cumbersome and expensive inhalers such as those of Clover, Bennett, Hewitt, Ormsby, Gwathmey, Junker and Vernon Harcourt (the last two for chloroform mainly). Clover's apparatus (Fig. 3)—as well as the three mentioned after it—consist of a bag, a receptacle for ether, a mixing

air admitted, or, sometimes, a breath of fresh air is allowed periodically after a given number of respirations in the inhaler. With these inhalers the ether vapor is warmed by the patient's expired air. A disadvantage, on the other hand, is that, in general, partial asphyxia is a factor in the anesthesia as well as the ether—an unfavorable circumstance during operations on enfeebled subjects.

The Junker inhaler (Fig. 4) as

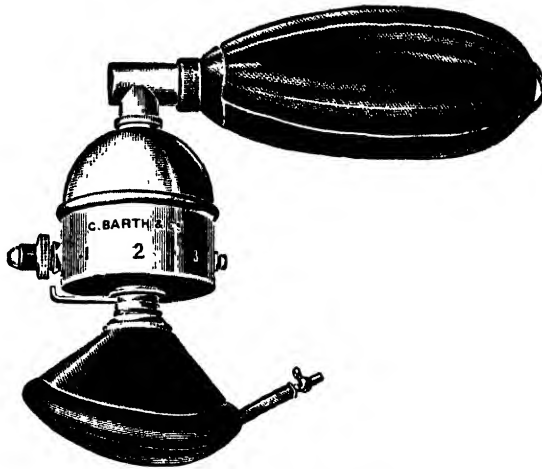


Fig. 3.—Clover's ether inhaler.

chamber, and a closely fitting mouth-piece with an inflatable rubber rim. With these inhalers the patient breathes immediately into and out of the bag, though openings for the entrance of fresh air are also provided. A regulating mechanism is supplied by which, after beginning with pure air, the patient can be made to breathe gradually increasing amounts of ether, the concentration of the vapor being mechanically under control and constantly adjustable to the desired percentage.

Where untoward symptoms, stertorous respiration or cyanosis, appear, the face-piece is lifted off and fresh

modified by Krohne consists of a vulcanite face-piece, connected by rubber tubing with a cylindrical graduated container for the anesthetic, this in turn being connected with a pair of rubber bulbs, by which air is blown through the anesthetic and then out into the face-piece. The Junker apparatus has been widely used, but is disadvantageous in that the closed mask is not sufficiently large to hold vapor for a full inspiration, and unnecessary work is thus thrown on both the respiratory and circulatory centers (Gwathmey). This danger can be overcome by attaching a thin rubber bag, to be con-

stantly two-thirds inflated with air, just behind the inhaler.

The same objection has been raised to the Harcourt inhaler (Fig. 5). This apparatus, moreover, is intended solely for use with chloroform, of which it supplies a vapor of accurately gauged concentration.

Gwathmey's apparatus for "vapor anesthesia" (Fig. 6) consists of a face-piece resembling an Esmarch mask but having a hollow rim, which is perforated with small holes to

to one that only penetrates the stopper. These tubes represent four different degrees of vapor strength. The percentage of the vapor varies according to the depth and temperature of the fluid in the bottles, the size of the hand-bulb, and the pressure with which the air or oxygen is forced through the tubes, either by the bulb or from an oxygen tank. There is no possibility of the patient's getting a vapor of dangerously high concentration. One can give

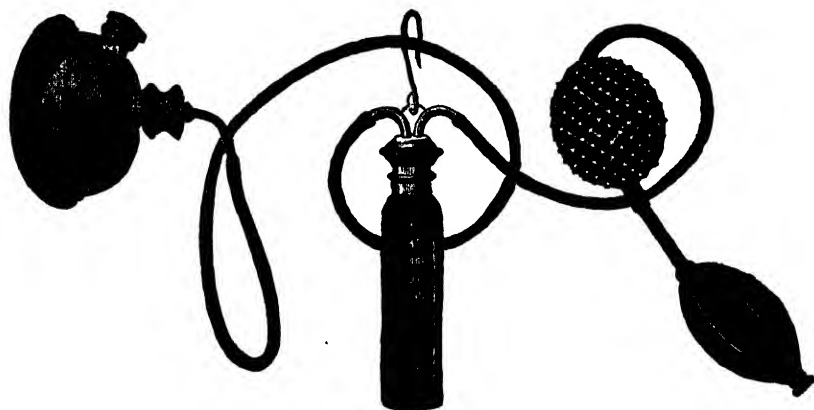


Fig. 4.—The Junker apparatus.  
(Medical Record.)

allow the vapor from the apparatus proper to escape under the mask and be respired by the patient. This mask is covered with 2 to 4 layers of gauze, over which is placed oiled silk or rubber tissue, provided with a central opening the size of a dime, so that during the period of induction a few drops of **chloroform** may be added, if necessary, in vigorous alcoholics. There are no valves in the apparatus, and therefore no re-breathing nor strained breathing at any time. In each of the three six-ounce bottles there are four tubes, varying in length from one that reaches to the bottom of the bottle

either a pure chloroform or ether vapor, or any combination of them, varying in intensity as circumstances require. In an emergency, oxygen can be given without disturbing the inhaler or the mask. Weak, anemic men, and the majority of women, can be anesthetized with the ether vapor alone. Changes from one narcotic to the other are done by simply turning a lever.

In the third bottle of the Gwathmey apparatus is placed, to render the induction stage pleasant, for a woman her favorite cologne, and for a man a highball or something similar. **Oil of orange** may also be used.

The anesthetic is started with a 1 per cent. vapor of cologne or whisky, and, as soon as the mucous membranes have become accustomed to this, a fractional per cent. vapor of chloroform is added for the first minute. This is changed gradually, but as rapidly as possible, so that at the end of three minutes the patient is getting 1 per cent. vapor of chloroform and a fractional per cent. of cologne or highball, after which the latter is turned off entirely. The average time to induce

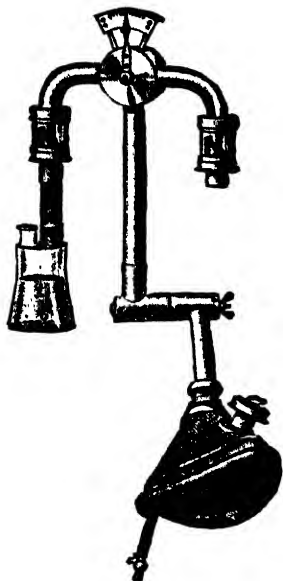


Fig. 5 —The Harcourt Inhaler.  
(Medical Record.)

surgical anesthesia is six minutes. The third bottle is then taken out, emptied, and refilled with hot water at about 100° F. (37.8° C.). When the chloroform or ether vapor is passed through this hot water, it is raised to the temperature of the blood, making it safer as regards life, and also more respirable, and still further reducing the after-effects. Or the cologne can be sprinkled on the mask, and hot water used from the first in the third bottle.

A very satisfactory method is to use the gas-ether sequence as a preliminary, and then allow the reflexes to become active, when oxygen-chloroform vapor is begun. Another method is to com-

mence with gas, then change to the vapor mask upon which 10 c.c. (2½ drams) of ethyl chloride has been poured, and continue with the chloroform vapor and air. After the operation has commenced, oxygen instead of air is allowed to flow through the chloroform. Still another method is to dispense with the gas and commence with the vapor mask, using ethyl chloride at the start.

An advantage of the vapor method of anesthesia is the fact that excitement is usually absent, or very slight. In the surgical stage the patient's breathing is regular and natural. The lid reflex is never entirely abolished, nor is there stertor or snoring or the mucous r le, even when giving pure ether. There is complete relaxation without the slow pulse of chloroform (as usually administered), or the billowy breathing and rapid, bounding pulse of ether. The total amount of anesthetic used is remarkably small. In the majority of cases there is absence of unpleasant after-effects. A continual narcosis is maintained without any danger to the patient.

Oxygen should be used whenever possible, especially with chloroform, as it has been proven that this combination is safer than ether and air. The author always uses chloroform and oxygen whenever and as long as possible, and continues the anesthesia with ether whenever this is indicated. The usual precaution of not giving ether in the presence of an open flame applies with double force to the more explosive mixture. The change from air to oxygen should not be made usually until the patient is well under the anesthetic and the operation has begun. J. T. Gwathmey (*Med. Record*, Oct. 14, 1905).

Description of an apparatus for narcosis under plus pressure. The apparatus is designed to allow the anesthetist to sit in the cabinet into which the head of the subject projects. This leaves the operator and his assistants free to operate under normal conditions, with access to instruments, etc. The large box or chamber is made light and

movable, and the ventilation is so contrived that the fumes of the anesthetic are conducted away without reaching the anesthetist. Engelken (*Deut. med. Woch.*, Dec. 15, 1904).

The writer recommends compression of the carotid arteries at the inner margin of the sternocleidomastoid muscles to hasten anesthesia with ether by producing cerebral anemia. Ritter (*Zentralbl. f. Chir.*, Sept. 8, 1923).

**General Management of Ether Narcosis.**—An important feature in anes-

the inferior border of the jawbone, and thus keep track of the pulse rate and volume; a mouth-gag and tongue forceps are seldom required when the jaw is correctly managed (Mellish).

The following method suggested as substitute for the painful mouth-gag and tongue forceps: With the head low, after opening the mouth with the gag, a broad, round, gauze pad, 3 to 4 cm. thick, held on a handle, is introduced on the side of the mouth opposite the gag. The introduction should be

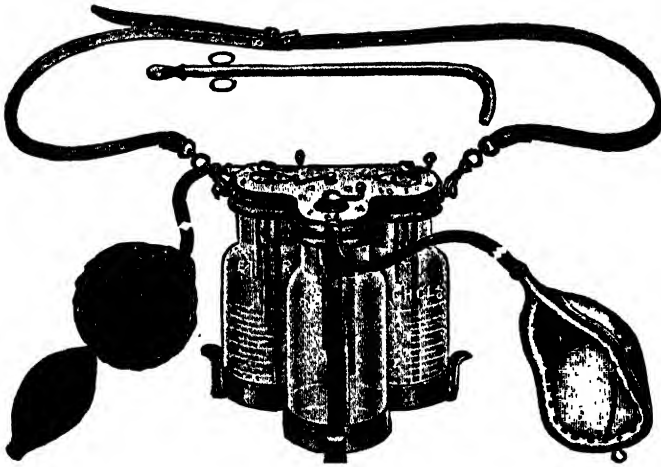


Fig. 6.—The Gwathmey vapor inhaler.  
(Medical Record.)

thesia is the management of the patient's jaw. It should be kept constantly forward, and this may be accomplished by placing the thumb on the malar prominence and exerting pressure from behind forward with the middle or ring finger under the angle of the jaw. As the muscles relax, the lower teeth may be hooked in front of the upper. At the same time the head should be rotated to one side and slightly extended—a position which removes the effect of gravity on the jaw and facilitates the passage of air through the larynx. One finger may be used to palpate the facial artery as it curves round

made with a rotating movement, so that the tongue is lifted forward. The pad is then rolled on the surface of the tongue until it rests on the base in front of the epiglottis, when the tongue will be resting on it. By drawing it in the direction of the submental region the tongue is lifted forward. The epiglottis follows this movement, and the larynx is kept open. It is easy to hold the instrument in this way during the whole operation, but this is rendered still easier by resting the shaft of the handle on the upper teeth. Since the pad gradually becomes saturated with mucus, it must be changed at times. When the pad and handle are in, the mouth-gag is not necessary and is removed. Gonterman (*Zentralbl. f. Chir.*, Bd. xxxviii, S. 1626, 1911).



When surgical anesthesia has been secured, the amount of anesthetic used should invariably be reduced, and, in fact, the aim throughout should be to administer as little of the drug as is compatible with the operative requirements.

During the opening of the abdomen and the walling off of the intestines full anesthesia is usually best. As soon as the operation proper is begun, the drug may be much diminished or even withdrawn for a time. During the closure of the peritoneum the amount may have to be increased, but the mask may usually be taken away after this and the rest of the incision closed without it. One likes to see a patient moving during the latter part of this process and talk while he is yet on the table. R. R. Smith (Phys. and Surg., March, 1910).

Very little of any anesthetic is needed to keep up any level of narcosis when the level is once established. When a narcosis is maintained without excessive interaction between the narcotizing agent and the tissues of the body, such tissues, even if temporarily damaged, will rapidly recover, provided their requirements—*e.g.*, adequate blood-supply—are safeguarded. D. W. Buxton (Lancet, May 11, 1912).

Where retching and vomiting occur during anesthesia, the patient's head should be tilted to one side, if it is not already in this position, in order to cause the regurgitated fluid—chiefly mucus and saliva—to recede from the air-passages. The mouth should be opened with the gag, if necessary, and the liquids present in it swabbed out with gauze sponges held in forceps. The vomiting is of no importance in itself, but is of great significance if the freedom of the air-passages is not constantly borne in mind, since aspiration of some of the ejected material may cause asphyxia. When the mouth has been opened

and cleared, it is well to draw out the tongue with the fingers (protected by a napkin or gauze) so as to facilitate the passage of air through the larynx by raising the epiglottis; or the index finger may be passed into the mouth back to the epiglottis, and the latter, together with the tongue, directly lifted forward.

If any degree of asphyxia shows itself, **Laborde's method** of stimulating respiration—traction on the tongue rhythmically, 15 or 18 times a minute—may be practised.

Excessive traction should not be exerted upon the tongue, for Crile has shown experimentally that this in itself is sufficient to cause a cessation of respiration, with fall of blood-pressure, etc. H. S. Wieder (Therap. Gaz., Dec., 1907).

Vomiting unattended by other untoward symptoms does not preclude continuation of the ether.

Embarrassed or arrested respiration, as well as marked excitement, in the earlier stages of anesthesia are best treated by temporary withdrawal of the anesthetic.

The question of proper regulation of the dosage of ether administered is one that must be continually before the anesthetist's mind, and is of paramount importance to the patient's interests. Contraction and immobility of the pupil constitute the chief sign that the proper degree of anesthesia is being maintained. Dilation, then, signifies either that there is danger or that too little ether is being given. But in cases where pupillary contraction does not occur, other indications have to be watched for, in particular those relating to the respiration, circulation, and color of the skin. Insufficient anesthesia is suggested usually by quick-

ened breathing, together with good skin coloration and circulatory activity. According to F. E. Simpson, the most valuable sign of beginning awakening of the patient is a lateral rolling of the eyeball from side to side, which precedes by some moments other evidences of returning consciousness. The rotation is slow and hesitating, and recurs at intervals of a few seconds; it signifies to the anesthetist that by adding a few drops more of ether from time to time he can prolong the proper operative condition for an almost indefinite period.

On the other hand, a suddenly dilating and subsequently immobile pupil, lividity of the face, and perhaps a pronounced increase in the pulse rate—from 90 to 120 or more—with diminution of the pulse volume and slowing and jerkiness of the respiration, indicate that the danger stage of anesthesia has been reached and greater caution in dosage is necessary. Cyanosis is frequently due merely to an insufficient allowance of air, which can readily be corrected, and is therefore less ominous than pallor, which tends to show, on the other hand, that circulatory activity is being gradually undermined by the drug.

There is a much greater interval of safety between the corneal reflex and the failure of respiration and heart than is generally admitted. Further, the reaction to corneal stimulation varies enormously in different individuals. The corneal reflex cannot be depended upon as a guide in the administration of anesthetics in cases requiring complete muscular relaxation, especially in abdominal and hemorrhoidal operations; in these, moderate secondary dilatation of the pupil, while keeping a careful watch on the respiration and pulse, is

the best guide. Gardner (*Brit. Med. Jour.*, April 22, 1900).

The conjunctival reflex is of little value in the majority of deeply etherized patients. The exceptional cases in which it persists are alcoholics and those with a full, hard pulse, as in chronic nephritis. The pupil reflex, however, is of great value in ether administration. The pupil of simple ether anesthesia is usually moderately dilated and round; it shows no immediate reaction to light, but if it be kept exposed, without further administration, it gradually contracts with jerky movements generally synchronous with the inspirations. In strong, muscular men; in those of either sex with hard pulses, alcoholics, and where **morphine** has been previously administered, the pupil approaches rather to the chloroform type. In deep etherization the pupil gradually enlarges till it is widely dilated, immobile, and usually irregular in outline. With this pupil in ether anesthesia there is a quiet, regular pulse and equally satisfactory respiration, and if the ether be withdrawn the pupils gradually contract to the moderately dilated, regularly outlined condition; the pulse and respiration continuing unaltered or but slightly accelerated. If administration be now not recontinued, there will eventually come a deep, sighing inspiration, which the author considers the best indication of all for more anesthetic. If it be not given the pupils continue to contract to the condition found in deep sleep, unless emesis occurs, when they become dilated.

One of the causes of the larger pupils in ether anesthesia as compared with chloroform anesthesia is the greater intraocular tension, due to the higher blood-pressure. A similar dilatation is temporarily caused by undue pressure over the cornea in ill-advised attempts to elicit a corneal reflex. Any but the gentlest touching of the conjunctiva is apt not only to damage the epithelium, but also quickly renders it less sensitive, and so diminishes the use of the test. Lawkins (*Austral. Med. Gaz.*, Jan. 20, 1903).

The diagnosis between pure respiratory and pure circulatory cyanosis is easily made by noting the capillary circulation. This is most readily done by compressing the finger-nails and noting the more or less rapid return of the expelled blood. Pedersen (*Med. News*, Dec. 31, 1904).

It is impossible under any known conditions for the respiratory center or the cardiac center to be poisoned by chloroform or ether while the upper eyelid still closes when the center of the cornea is touched by the finger. The administrator, standing behind the patient, inserts the pulp of his middle finger between the palpebral edges, drawing the upper eyelid upward and at the same time brushing that finger-pulp lightly against the center of the cornea. When he has arrived at the upper limit of the pupil he should let go altogether, noting both by the senses of touch and sight the degree of briskness with which that upper eyelid closes. When a definite difference exists in the activity of the two upper eyelids, one must be guided by the more active.

Pupillary signs may be neglected altogether. A progressive dose of chloroform or ether having been given until the upper eyelid is weakly active in response to corneal contact, this condition can be exactly retained throughout by stopping the anesthetic for a few breaths to quicken its activity, or giving more anesthetic to weaken it as required. As to the air-ways, it is necessary to know by the sound of the breathing when they are clear. Every expiration must be either heard or felt, to make sure that efficient breathing is going on. It is of no use to see the abdominal and thoracic movements, for they may proceed for a considerable time after obstruction to air entry has taken place. Duskiness of the lips and ears is a sign that air is not entering the lungs in adequate amount. The administrator should put in a small mouth-prop, raise the jaw or draw the tongue forward, directly the sound of breathing through clear air-ways is replaced by that of partially obstructed respiration.

Gardner (*Brit. Med. Jour.*, June 5, 1909).

A stertorous respiration suggests either an excess of anesthetic or an obstruction to breathing, such as mucus, falling back of the tongue, or laryngeal edema. That one of the latter causes is active can usually be determined without difficulty upon investigation. Holding the jaw well forward, as already described, and drawing on the tongue, are useful diagnostic procedures in this connection. The anesthetist should bear in mind that visible respiratory movements of the chest do not necessarily certify to the entrance of air into the lungs, and should therefore be on the alert for any indication of respiratory difficulty; otherwise, the patient may be unwittingly allowed to pass into a condition of serious respiratory depression.

There are many ways in which the respiratory passage may be obstructed. A large thyroid may press on the trachea till respiration is difficult when the patient is conscious, and insufficient when ether is given.

Vigorous efforts on the part of the surgeon removing an enlarged thyroid or glands of the neck may cause cessation of respiration, either from constriction of the trachea or possibly through vagus inhibition.

The risk of giving ether to persons suffering from cellulitis of the neck should always be remembered, for in severe cases of this kind there is generally coexistent edema of the larynx, which may be increased by the effect of ether till it produces asphyxia. Even then, when laryngotomy is performed quickly, the patient's life will generally be saved.

Asphyxia may be caused by the inspiration of vomited matter, most frequently in cases of intestinal obstruction in which the vomiting is almost continuous, and in large quantities. By keeping a pillow under one shoulder,

however, the vomit may generally be made to run out of the mouth. R. J. Probyn-Williams (*Clinical Jour.*, Dec. 23, 1908).

Case of nitrous oxide-ether anesthesia complicated by bronchorrhea. The pulse increased in rapidity and lost volume, the respirations became shallow and irregular, and the patient cyanotic. The moment the ether was withheld the patient promptly offered resistance, and when more was administered his breathing was interfered with. The author ordered a 5 per cent. solution of **epinephrin** 1:1000, diluted 1 to 20, and with this mopped out the pharynx. Almost immediately the secretion of mucus became less, the respirations clearer and deeper, and the patient less cyanotic. The author then used epinephrin in anesthesia as a routine in a series of cases. He found that a 25 per cent. aqueous solution of the standard 1:1000 gave the best results. Pouring ether in the towel cone and spraying the epinephrin solution on it, depending on the ether to vaporize it sufficiently for inhalation, is the best mode of administration. Three- to six- minute intervals are sufficient for its use, and a total of from  $\frac{1}{2}$  to 1 ounce of this solution is enough for an operation lasting from thirty minutes to an hour. The effects are a more uniform etherization, the pulse becoming steadier and slower. The respirations are quiet and regular, and the bronchial secretions are practically checked. Recovery from the anesthetic was uniformly good.

The epinephrin, acting generally from absorption, is a powerful stimulant; it materially lessens shock, lessens the capillary ooze at the field of operation, and is of great benefit to the much weakened patient. Venable (*Va. Med. Mthly.*, Feb. 22, 1907).

Within a reasonable limit, quality, not rate, is the consideration in observing the pulse; and depth, not rate, of the respiration. As to the pupil, one should use it more as an arbiter when it is necessary to decide between two seemingly opposed factors, or to decide the importance, when otherwise all seems well, of the presence of cer-

tain conditions, as cyanosis, stertor, continued rigidity, or an increasing rapidity of pulse, or shallowness of respiration.

The presence throughout anesthesia of stertor or a slight degree of cyanosis need not alarm unduly, but should cause increased watchfulness, since its presence is always indicative of obstruction to the passage of air, though such interference may be exceedingly slight. Many of the more plethoric exhibit cyanosis from the induction and throughout the anesthesia without apparent significance, but in the arteriosclerotic cyanosis is apt to be the precursor of danger.

Respiration simply rapid, say 30 or 40, need seldom be viewed with gravity, but not so any irregularity or rhythm or extreme shallowness. Preceding the return of reflexes with accompanying vomiting there may be an apparently unexplainable change for the worse in the pulse. It is in such cases that reference to the eye is of much value.

Laryngeal spasm may be avoided or be generally overcome without difficulty in the initial stage by the free admission of air. But the occurrence and recurrence of this spasm during deeper anesthesia may be prophetic of trouble. In such, air should not be restricted and ether very cautiously given. If the free admission of air does not overcome the spasm, the jaws should be pried apart and the tongue forcibly drawn forward. J. B. Bogan (*N. Y. Med. Jour.*, Sept. 24, 1910).

It is neither wise nor necessary to obtain a degree of anesthesia free from all reflex movements of the thighs for **circumcision** in childhood; but, having weakened the corneal reflex, it is well to get the nurse to place her hand on the patient's knees to prevent their upward reflex movement when the prepuce is first seized. Reflex laryngeal crowing almost always arises also at this moment, and the lips should then be rubbed briskly with a towel to stimulate deeper breathing; the jaw should be pushed forward and the anesthetic withheld until respiration is more

regular. In operations for **adenoids** and **enlarged tonsils** it must be borne in mind that patients with these affections have more or less obstructed air-passages, and that the operation and the bleeding it causes also cause intermittent respiratory obstruction. Gardner (Brit. Med. Jour., June 5, 1909).

In chronic alcoholic or nervous patients, considerable difficulty is not infrequently experienced in inducing proper anesthesia. In such cases the cautious administration of chloroform for a short time will often prove effectual. In "florid" individuals in general, a fairly deep anesthesia is usually to be maintained, in order to avoid troublesome reflex manifestations. In obese subjects it is particularly necessary that there be no insufficiency of air-supply; hence the "closed" methods of ether administration are by many considered inadvisable for such patients. The anesthetist should remember that after the breathing has temporarily ceased owing to reflex irritation, or when in the operation sensitive or inflamed tissues are being dealt with or the anal sphincter is being stretched, deep respirations occur which tend to increase suddenly and markedly the amount of ether taken into the patient's lungs. Some degree of caution as to the quantity of ether supplied under such circumstances is therefore required.

Muscularity often causes delay and difficulty in anesthetization, and as a large number of fatalities from chloroform have occurred in patients of this type, ether should be chosen wherever possible rather than chloroform. Generally, a mixture of **chloroform** and ether, administered slowly, gives better results than ether or chloroform in muscular and obese subjects. Patients confined to bed for a considerable time owing to some constitutional disease

are not, as a rule, bad subjects for anesthesia. Hewitt (Lancet, Jan. 10 and 17, 1903).

Patients meeting with an accident causing dislocation of a limb are unprepared by abstinence from food for an anesthetic, and are not likely to take it well. A jaw-gag must be at hand in case of semisolid vomiting, and whatever anesthetic is used to make the patient unconscious, ether should afterward be given to obtain muscular relaxation. A great many deaths have occurred under chloroform unwisely pushed for this purpose. C. E. followed by ether or gas and ether are the most valuable and safe anesthetics to employ. Gardner (Brit. Med. Jour., June 5, 1909).

The **nitrous oxide** and **oxygen-ether-chloroform** sequence may be employed to eliminate the dangerous induction period of chloroform anesthesia when it is desirable to employ that anesthetic. W. H. Allen (Jour. Amer. Med. Assoc., Nov. 11, 1911).

The fact that ether is easily ignited should always be borne in mind.

The writer reports the following unusual experience: While engaged in a tedious and difficult operation, his attention was taken from his work by a sudden flash of light and some quick movements on the part of the anesthetist. The ether vapor had ignited, scorching the hair and eyebrows of the patient, and had burned the skin on his forehead sufficiently to cause quite a marked redness. The anesthetist reported that the patient being on the face, he was unable to see the pupil properly, and he had turned on the electric light in order that he might more readily note the reaction of the pupil. The blaze had occurred coincidentally with the turning on of the light. There was no exposed fire in any part of the operating room, and the only conclusion was that the vapor of ether had ignited from the spark in the electric light burner made when contact took place in turning on the light.

It is well for any surgeon or anesthetist not to turn electric lights on or off

near ether vapor, particularly when the room is small and there is a large amount of the vapor in it. Yet it is not so easy to produce a blaze by the turning on of an electric light in the presence of ether when one tries it for that purpose. Since the above occurrence, the author has tried the experiment several different times in different ways, with the same burner and others, and has been unable to produce a blaze with ether vapor. Thus, while it is possible that this experience may be unique, and it is certainly of rare occurrence, every surgeon and anesthetist should bear in mind the fact that it has occurred. Very serious consequences might easily have resulted in this case if the anesthetist had lost his head. D. H. Murray (N. Y. Med. Jour., June 27, 1903).

**Postanesthetic Precautions.**—After the patient is removed from the warm operating room, it is of the greatest importance that he be protected from cold and draughts of air while being removed to bed. The bedroom and the bed should be warm. Aspiration pneumonia should be guarded against by seeing that the patient does not unnecessarily inspire vomited material into the trachea. The system should be amply supplied with fluids, either by stomach, by rectum or subcutaneously, in the form of normal saline solution, and as much nourishment should be given as conditions permit (Mellish). The suggestion has been made that the patient be required, wherever possible, to breathe deeply for a period after the anesthesia, in order to hasten the elimination of the drug from the system and minimize any harmful effects to which prolonged contact of it with the visceral parenchymas may give rise.

The writer places his patients in a sitting posture immediately the operation is finished, no matter what

the condition operated for, and almost never witnesses vomiting or nausea. He ascribes this to the avoidance of congestion in the medulla and also to the fact that pressure of the abdominal viscera is removed from the diaphragm by gravity. Chandler (Surg., Gyn. and Obst., Nov., 1911).

Following points relating to anesthesia emphasized: Never use alcohol as a stimulant during or after an anesthesia if the opsonic power of the blood is of any importance. Make the anesthesia as short as possible. Take special precautions for asepsis and antiseptics in all operations of any length. A very slight infection, which would not manifest itself under ordinary circumstances, may develop into a serious condition after an anesthesia. Inject slowly 6 ounces (180 c.c.) of pure limpid olive oil high up into the rectum in all septic cases, and in all others in which the power to resist infection may be called into play. Ferguson (N. Y. Med. Jour., May 11, 1912).

Study of 40 cases has shown that the use of **carbon dioxide** to accelerate **deëtherization** by stimulating respiration confers the following benefits: (a) The volume of respiration can be raised to any desired level; (b) recovery of consciousness is from three to five times more rapid; (c) blood-pressure, circulation and color are materially improved; (d) nausea, vomiting and other subjective disagreeable sensations following ether anesthesia are reduced. Other indications for the use of carbon dioxide as a stimulus to respiration are: (a) In cases in which the respiratory center is depressed by direct pressure or injury; (b) in the treatment of failing respiration during the period that ether is given. In no instance have any signs of acidosis or other harmful effects attributable to carbon dioxide been noted. White (Annals of Surg., Sept., 1923).

**UNTOWARD EFFECTS.—A.**  
**During Anesthesia.**—**Respiratory arrest** may occur as a primary effect of the administration of an excess of ether. In the early stages it is due to

irritation of the mucous membranes and is relieved by temporary removal of the anesthetic, supplemented, if necessary, by **artificial respiration**.

Breathing may cease during surgical anesthesia (*a*) from the presence of muscular spasm or some other condition within the air-passages, causing occlusion; (*b*) from some external agency preventing lung expansion; (*c*) from a diminution or arrest of the blood-supply to the respiratory centers; and (*d*) from the toxic effect of the anesthetic upon those centers. A frequent cause of difficulty in inducing and maintaining anesthesia is the presence of partial or complete nasal obstruction. Whenever practicable, oral breathing should be secured and maintained in preference to nasal breathing, for the latter is often inadequate, retarding the onset of anesthesia and leading to hyperpnea, venous engorgement, and abdominal rigidity. By the most careful attention to symptoms the anesthetist may, in the great majority of cases, and particularly toward the close of operations, permit the patient to display a slight trace of corneal reflex. Hewitt (Lancet, July 20, 1907).

Later in the anesthesia, however, it is due to the direct effect of an excess of ether on the respiratory center, and is likely to be accompanied by dilatation of the pupils, loss of the conjunctival reflex, and soon after by cyanosis and objective evidences of secondary circulatory enfeeblement.

The *treatment* of the latter form of respiratory arrest consists in **immediate removal of the anesthetic, lowering of the head of the operating table, and artificial respiration**.

Case of total respiratory failure from ether following an operation for appendicitis. **Artificial respiration** was practiced for over four hours, and various stimulants were also used, followed by recovery. The only agents which seemed to be of service

were artificial respiration and **adrenalin chloride**. Discontinuance of artificial respiration always produced cyanosis. Renewed efforts restored the color of the skin. To the adrenalin chloride belongs the greater part of the credit of resuscitation. It lowered the beat of the heart to nearly normal and increased its power and volume. At no time after the first dose of 30 minims (1.8 c.c.) did the action of the heart fail. It was administered the day after the operation in doses of 10 drops every two hours. This drug, in the writer's experience, is the one valuable thing in cases of cardiac failure from shock and hemorrhage. H. H. Everett (Medical Record, May 23, 1903).

**Rhythmical tractions on the neck** have exactly the same effect as the rhythmical traction on the tongue. The maneuver consists in standing behind the head of the patient and then stretching the neck backward and forward twenty or thirty times a minute. Depage (Jour de Chir. et Annales de la Soc. Belge de Chir, Jan., 1904).

**Collapse**, implying primarily a weakening of the circulatory rather than the respiratory functions, is less likely to occur under ether than under chloroform. Sudden cardiac paresis and inhibition, such as can readily be produced by incautious administration of chloroform in the early stage of induction, is a comparatively rare event in the case of ether. Circulatory weakening from the latter drug more characteristically occurs after prolonged complete surgical anesthesia. The pulse is observed gradually to become feeble and irregular, dilatation and immobility of the pupils are noted, pallor or cyanosis appear, and the heart action may ultimately completely stop—synchronously with, or only slightly preceding, respiratory enfeeblement and arrest. The condition present is one of cardiac dilatation and likewise vascular dilata-

tion, the vasomotor center being generally simultaneously impaired.

The *treatment* of collapse consists in **stopping the ether, raising the feet, and lowering the head**—in order to improve the blood-supply to the bulbar centers,—instituting **artificial respiration** to prevent further weakening of the heart through imperfect oxygenation and favor removal of ether from the system, and the application of various stimulant and other supporting measures. **Oxygen inhalations** should be at once instituted. **Forcible compression of the heart** with clenched fist, 120 times a minute, through the chest-wall, is likely to prove of value, where there is no abdominal opening, in emptying the overburdened heart, and may even be employed with the idea of creating an artificial carotid pulse. In abdominal operations **massage of the heart** may be practised by inserting one hand in the peritoneal cavity and rhythmically squeezing the heart through the relaxed diaphragm between the thumb and finger, or compressing it between the inserted hand and the other hand placed on the precordium externally. These compressions should be repeated 20 to 40 times a minute. Mechanical cardiac stimulation has also been effected with a finger passed through an incision in the chest wall, in the fourth intercostal space.

A patient who had withstood one hour of chloroform-ether narcosis without trouble, suddenly went into complete collapse. Trendelenburg posture, artificial respiration, oxygen and hypodermic stimulation failed to restore. When no signs of life were obtained for five minutes subdiaphragmatic **massage of the flabby heart** was begun in combination with the other measures. After two minutes the heart

grew firmer and a few cardiac and respiratory movements were noted, but when the massage was stopped complete syncope returned. The massage was resumed and the heart responded after one minute. Gradually the heart began to recover, and all the vital functions slowly returned. The patient recovered from the operation. A. T. Jurasz (Münch. med. Woch., Jan. 10, 1911).

In a large percentage of patients succumbing to primary cardiac failure under ether there has, in all probability, been no real heart disease and no status lymphaticus, but an acute susceptibility equivalent to these conditions has been developed by unskillful anesthesia. A fatality of this class seldom occurs after profound and prolonged anesthesia. It is especially the sequel of light anesthesia.

Usually the printed accounts of such cases state expressly that the administration of ether was interrupted once, or twice, or several times, thus allowing the subject to come nearly out of anesthesia. The patient may even have winked his eye only a few seconds before the circulation suddenly failed. He may have drawn deep, gasping breaths some time after the heart had completely stopped beating. Quite often the case is that of a child under operation for adenoids.

This form of death and, in fact, by far the greater number of all deaths under anesthesia are fundamentally due to acapnia resulting from the excessive pulmonary ventilation of the stage of excitement. Experimental evidence shows that acapnia exerts deleterious effects upon the heart, and upon many other functions, no less than upon respiration. Dogs which have not been excited at any stage usually take chloroform well. If one gives too much chloroform, respiration usually stops some time before the heart. If, on the contrary, the subject has first been rendered acapnic, the hypersusceptibility thus produced renders even the strongest animals liable to sudden primary car-



diac failure under an otherwise moderate dosage of chloroform. Y. Henderson (Surg., Gynec., and Obstet., Aug., 1911).

**Venesection** has been practised to relieve engorgement of the right heart due to high vascular tension.

Other valuable measures include the intravenous injection of warm **saline solution**, to which a few to 20 drops of 1:1000 **epinephrin** solution are — preferably gradually — added, **bandaging of the limbs and abdomen** to compensate for vascular relaxation and improve the blood-supply to the centers and heart, and **external heat**, applied by means of hot blankets and water bottles.

Experimental research on resuscitation of dogs killed by anesthetics showed that **Ringer's solution** yields more favorable results than saline solution. The most satisfactory results were obtained with the infusion bottle at a height of five or six feet. Crile and Dolley (Jour. of Exper. Med., Dec. 21, 1907).

Drugs, such as **strychnine** ( $\frac{1}{20}$  grain — 0.003 Gm.), **digitalis** (10 minims — 0.6 c.c. — of fluidextract), **atropine** ( $\frac{1}{100}$  grain—0.00065 Gm.), **caffeine sodiobenzoate** (8 grains—0.5 Gm.), and **cocaine** ( $\frac{1}{4}$  grain—0.016 Gm.), sometimes do not prove of immediate service in combating the circulatory depression, but are useful to maintain cardiovascular activity once it has been partially restored by other measures. Injections of sterile **camphorated oil**, 20 minims (1.25 c.c.), may be given. Alcohol is of doubtful value, and the nitrites are to be eschewed. **Rectal injection of warm coffee** constitutes a useful measure.

**Shock**, consisting essentially of vasomotor exhaustion, with cardiac enfeeblement, if present, only

a secondary manifestation, is to be differentiated from collapse due more directly to the anesthetic. It may come on during an operation and persist after it is ended, and may be due either to overstimulation of the nervous system the result of excessive tissue injury during the operation (Crile), to hemorrhage, or to exposure to cold. The symptoms consist of pallor, sweating; a soft, irregular, and accelerated pulse (especially if there has been much hemorrhage), and respiration that is at first deep and sighing, then feeble. Shock is distinguished from the effects of an overdose of the anesthetic by the persistence of the corneal reflex, through an appreciation of the severity of the operation, and by consideration of the preceding depth and duration of anesthesia, the anesthetist judging the probable effects of the amount of anesthetic already used.

Respiratory surgical shock is most common during light or moderate anesthesia, before the corneal reflex has vanished; while circulatory shock, which is by far more common under chloroform, is met with during profound narcosis. Respiratory shock is specially liable to complicate operations upon the rectum, urethra, abdominal organs, uterus, perineum, and kidney. The immediate cause is usually a reflex spasm affecting either the tongue, fauces, palate, and adjacent parts, and having stertor as its audible expression; the larynx, and producing stridor; or the respiratory muscles, and bringing about respiratory spasm. Circulatory shock is chiefly met with in operations on parts possessing important nerves or rich in nerve-supply. The immediate cause is usually a sudden relaxation or paralysis of the vasomotor system, generally associated with some cardiac inhibition. The favorable conditions for the establishment of respiratory shock

are partial anesthesia, manipulations upon sensitive parts, and the presence of an air-way likely to become occluded. Those for circulatory shock are deep chloroform anesthesia, the horizontal, semirecumbent, or sitting posture, and intestinal, omental, uterine, or renal traction. Simple chloroform overdosage may be indistinguishable from circulatory shock. Respiratory shock may usually be avoided by securing full anesthesia before the patient is moved, and by so adjusting the degree of anesthesia that reflex modifications in respiration are as far as possible eliminated. Circulatory shock can be avoided by using ether instead of chloroform; if the latter is used, too deep anesthesia must be avoided, and the patient placed in the Trendelenburg posture, in which position circulatory shock is almost never seen.

The treatment of respiratory shock is to re-establish respiration as soon as possible by separating the clenched teeth, sponging out the fauces, pushing the lower jaw forward, **tongue traction**, **artificial respiration**, and, if need be, **laryngotomy** and direct **lung inflation**. The treatment of mild circulatory shock is to lessen the depth of anesthesia and to substitute a chloroform-ether mixture, or ether for the chloroform. When severe, the anesthetic must be withdrawn, the **head lowered**, the **feet raised**, and **artificial respiration** be performed. Unless the patient be very deeply anesthetized recovery can be effected very rapidly, and the operation proceeded with. Drugs are of little or no value. Hewitt (*Lancet*, July 27, 1907).

The *treatment* involves both prophylaxis and the application of active measures when the condition has already become established.

The treatment of surgical shock and collapse should be very largely by prophylaxis. The anesthetist should give as little anesthetic as possible. In certain brain and abdominal cases the operator and the anesthetist should work together, the depth of the narcosis

increasing and diminishing as indicated by the operative manipulations. The anesthetist should notify the nurse to prevent any unnecessary exposure of the body. The "nerve-blocking" procedure of Crile should be used to lessen the shock, when operating on an extremity. The large nerve-trunks are cut down on after anesthesia and are injected with 4 to 10 minims (0.25 to 0.6 c.c.) of 4 per cent. cocaine. Caswell (*Boston Med. and Surg. Jour.*, June 28, 1906).

Wherever shock is seen to be present before operation, *e.g.*, where the patient has been severely injured in an accident, an injection of **morphine**, together with infusion of **saline solution** and **epinephrin**, will serve as prophylactic procedures.

Where shock develops during an operation, drugs such as **pituitary extract** and **digitalis** should be administered, and many of the measures already described under Collapse—**lowering of the head**, **external heat**, **bandaging of the limbs and abdomen**—brought into requisition. **Crile's pneumatic suit**, serving the same purpose as bandaging, may be used with marked advantage, if available.

**Adrenalin** is the only drug to be used in true surgical shock. It should be given with saline solution by intravenous infusion. The proportions of adrenalin are, 1:1000 solution, one part in 200,000 parts of saline solution. Salt solution, when given alone intravenously under the skin or by rectum, is of little or no benefit in cases of shock, as it does not raise the blood-pressure. All other stimulating drugs, as strychnine, are out of the question for the same reason. In collapse drugs may be employed with advantage, because the vasomotor center needs and can take stimulation to bring it to its proper condition. **Strychnine** may be used. **Alcohol** is of some value, but its stimulating effect is due to the chemical irritation it causes. **Cold**

**water on the face, ammonia fumes, and artificial respiration** will do the work. **Salt solution** is indicated if the collapse is due to loss of blood. When shock and collapse are combined, the outlook is unfavorable, but treatment should be along the lines of shock. Caswell (Boston Med. and Surg. Jour., June 28, 1906).

In cases in which shock is not due to hemorrhage, in the earliest stages, the condition can at times be met by the hypodermic administration of **camphor** 1 grain (0.065 Gm.) in oil, **digitalis** 15 minims (1 c.c.), or 15 minims (1 c.c.) of **epinephrin chloride**.

Unless the circulatory failure is distinctly due to cardiac disease and not to vasomotor exhaustion, as is usually the case, strychnine should be avoided, for in shock, as shown by Crile, strychnine rather aggravates than alleviates the condition. Should the skin be leaking badly, the administration of **atropine sulphate** grain  $\frac{1}{400}$  (0.00065 Gm.) will assist materially.

In some cases all these measures appear to be insufficient and the patient sinks rapidly. At this juncture nothing will tend to revive her as speedily as the slow, continuous intravenous introduction of about 500 c.c. (1 pint) of normal **saline solution** with **epinephrin chloride** 15 minims (1 c.c.), to be followed immediately by the subcutaneous introduction of 1000 to 2000 c.c. (1 to 2 quarts) of salt solution.

In cases of profuse hemorrhage, in addition to lowering the head of the patient, the author employs the same measures, but instead of introducing 500 c.c. (1 pint) of normal saline solution with epinephrin chloride, 1000 or 1500 c.c. (1 or 1½ quarts) are slowly introduced intravenously. One should never try to cut the vein with a knife, but always use a scissors, making a clean cut in a transverse direction.

The most efficient method for combating shock and raising the blood-pressure is the **pneumatic suit of Crile**, but this is rarely at hand.

**Bandaging of the limbs** tightly from the extremities upward will in some degree answer the same purpose. **Hot-water bottles** and **hot blankets** should be placed around the patient, and every portion of the body but the operative field should be kept covered and dry. H. S. Wieder (Therap. Gaz., Dec., 1907).

Saline solution must not be pushed if there is hemorrhage which is not yet under control; otherwise more blood may be washed out of the vessels and the condition made worse. If hemorrhage is not a factor **saline infusion** is, on the other hand, an essential measure. The best procedure of all for severe shock, but one not often possible, is **transfusion of blood**: Blood remains in the vessels, whereas saline solution soon leaks out into the tissues.

**B. After Anesthesia. — Vomiting** is a very common after-effect of ether anesthesia. Usually it soon ceases, but in some cases it tends to persist for a number of hours or even days. The incidence of vomiting depends to a considerable extent upon the care with which the patient is prepared for anesthesia and the pains taken to avoid overdosage of ether. In incomplete anesthesia, changing the position of the patient may bring on retching and vomiting.

Accompanying disease is a frequent cause of vomiting. In such cases, if practicable, the operation should be deferred until a suitable time. In persons of a nervous temperament more vomiting ensues upon anesthesia. It is of the utmost importance to have the patient in as peaceful a frame of mind as possible. The room should be absolutely quiet.

In winter time it is best to warm the anesthetic. To do this the author uses a half-glass of hot water and places the bottle into that. The water is changed

when necessary. By this method much less anesthetic is used and complete anesthesia is obtained much more quickly.

Uneven anesthesia should be avoided. There is more vomiting from five minutes of an irregular anesthesia than from one hour of an even one. Excessive stimulation by hypodermic injections during anesthesia may be a contributing cause of vomiting.

To diminish the salivary secretion the author rolls up two small hand-sponges and places one in each buccal cavity opposite the second molar tooth (the exit of Stenson's duct). In this manner all the secretions of the parotid gland are stopped. To prevent the patient from swallowing the sponges or the anesthetist from forgetting to remove them, a string may be attached to each sponge and allowed to hang down from the corners of the mouth.

It should be remembered that all body movements increase vomiting—especially so *after* anesthesia. The best method to control postanesthetic vomiting is to keep the patient without moving, in a quiet room, and to administer very small quantities of **hot water**, or very small pieces of **cracked ice**, at frequent intervals. J. Halperin (N. Y. Med. Jour., July 22, 1911).

Vomiting is due to either irritation of the gastric mucous membrane or it may be due to brain conditions or renal conditions. When it arises from cerebral or cerebellar conditions it may be due to the head having been kept at too low a level. Unless there is obvious ischemia of the brain, prolonged depression of the head, especially in plethoric persons, will tend to produce postanesthetic sickness. As soon as the patient has come through the operation, if he is not greatly collapsed he should be kept fairly raised.

Vomiting from the stomach may be due to imperfect preparation of the patient. If the patient is not starved to excess, has no purge for two days before the operation, and has the bowels properly regulated, such vomiting is avoided. In the case

of a person who is known to be inclined to vomit, the best plan is to feed by the rectum for twenty-four hours before the anesthetic and to allow copious libations of hot water for three days before.

Renal vomiting is a very serious condition. It is due in general to the operation, though it may be also due to too much anesthetic. Buxton (Clinical Jour., April 24, 1912).

The liability to vomiting is increased when acetone is found in the urine. Protracted vomiting is best treated by **sodium bicarbonate** by bowel and by lavage. These patients need careful watching on account of the liability to acid intoxication. Acetonuria is due to faulty metabolism, and increased by carbohydrate starvation. It has no relation to the length of anesthesia. The duration of anesthesia has only a slight influence on vomiting. Chalfant (Jour. Amer. Med. Assoc., Sept. 14, 1912).

The author does not believe that the presence of ether in the stomach is the cause of postanesthetic nausea. Even if it does, olive oil, as often recommended, can do but little good, for it finally becomes saponified and is absorbed as any other digested fat, possibly carrying into the system again with itself some of the ether to be re-excreted, and liberating a part to play again the rôle of irritant. A better agent is **liquid petrolatum**, which is inert, cannot be saponified and absorbed, and is an excellent protective to mucous membrane. Ferguson (N. Y. Med. Jour., June 29, 1912).

*Treatment.*—Vomiting during anesthesia can often be controlled by prompt **pressure** with the thumb or finger on one of the **phrenic nerves**, viz., posteriorly above the clavicle between the two heads of the sternocleidomastoid muscle, the head being meanwhile turned to the opposite side (Joos).

Vomiting after conclusion of anes-

thesia may be treated by frequent **rinsing of the mouth with ice-cold water**, by giving the patient small pieces of ice to suck, or by administering teaspoonful doses of very **hot water**. **Inhalations of vinegar** have also been advised, but are less efficient than the preceding.

The most satisfactory method of controlling nausea and vomiting after anesthesia is the administration of strong **vinegar by inhalation**. A towel or cloth, saturated with fresh, strong vinegar, is held a few inches above the patient's face, or hung from the bedstead, so that it will be near his head. Rugh (Dunglison's College and Clin. Record, April, 1898).

Bile being alkaline in reaction, when from relaxation or reversed peristalsis it enters the stomach, though this organ be at rest and therefore covered with mucus, causes an outflow of gastric juice. The acids are set free, with a resultant fluid vomit easily capable of burning the skin. Burns may occur on the mouth and cheek after vomiting of strongly acrid bile-stained fluid. The anesthetist should have at hand a towel saturated with **weak soda solution** to wipe any part touched by vomited matter. Griffith (Med. Record, April 19, 1902).

**Gastric lavage** is a valuable measure in severe vomiting. Some, in fact, advise its routine use before the patient regains consciousness. It is performed by passing a rubber stomach-tube through the nose or mouth and running in one or two quarts of normal saline solution, the patient's head being meanwhile lowered to prevent returning fluid from entering the trachea.

Ether is excreted largely by the gastric mucosa, and as long as this is kept up vomiting may occur. By prolonged **lavage** the ether is washed out of the blood and vomiting is prevented. The tube is kept in the

stomach and that organ thoroughly washed out before the patient recovers from the anesthesia. Two and a half or three gallons of water are introduced into the stomach and siphoned out, a pint or a quart at a time. If the patient has nausea after ether he is required to drink a glass of water. Brown (Surg., Gynec., and Obstet., Aug., 1905).

To prevent fecal vomiting during anesthesia, **lavage** may be employed, and the stomach and esophagus cleaned out with **boric acid solution** and hot water. The next step is to perform **laryngotomy** under local analgesia, or even under light anesthesia. As soon as the larynx is opened, and a **cocaine spray** used to lessen spasm, **chloroform** is to be administered through the laryngeal tube to full anesthesia. The mouth is opened by a gag and a full-sized **esophageal tube** introduced into the stomach. After packing very carefully both the upper opening of the larynx and the pharynx around the esophageal tube, the free end of the esophageal tube must be allowed to drain into a vessel containing a deodorant and antiseptic. It is essential that the tube be introduced and maintained in the stomach, and that the packing round it be tight Buxton (Brit. Med. Jour., April 23, 1910).

A simpler method of washing the stomach is merely to have the patient drink a glass of **hot water**, which will wash out irritants from the stomach when the patient vomits.

Other measures recommended to allay vomiting are the placing of a **hot-water bag**, **ice-bag** or **mustard plaster** over the stomach, the repeated administration of  $\frac{1}{12}$  to  $\frac{1}{8}$  grain (0.005 to 0.008 Gm.) of **cocaine hydrochloride** in a teaspoonful of hot water, the giving of **sodium bicarbonate**, 15 or 20 grains (1 to 1.3 Gm.) in a glass of warm water, the use of gastric sedatives such as **bis-**

**muth subnitrate** and **cerium oxalate**, and, finally, general depressant drugs such as **acetanilide**, **bromides**, and **morphine**. Buxton has recommended the administration of a mixture of 4 or 5 drops of **chloroform** with 2 or 3 drops of **vinegar of opium**.

If, as a cause of vomiting, there has been swallowing of blood or mucus, or there is complaint of the taste of ether, it is best to give a half-pint of **hot water** containing a teaspoonful of **sodium bicarbonate**. This will probably either wash out the stomach into the bowel or cause an effectual and final vomit. It may, however, be necessary to repeat it after an interval. **Black coffee**, to which some add **sodium bicarbonate**, also **iced champagne** in small quantities, have seemed to do good. The taste and smell of ether may be overcome by the use of thin slices of **lemon** and of toilet **vinegar**. For neurotic patients a **mustard leaf on the epigastrium** may be recommended with confidence. When vomiting threatens to be severe or continuous, a detailed examination of the urine should be made, especially after interference with any part of the urinary tract and when acid intoxication may be suspected. If there is atonic distention, **strychnine**, **pituitary extract**, or **ergotine** (hypodermically) is often effective, and the bowels should be well cleared out by **enemata**, if not acting. A rectal tube may be left in for an hour or so at a time and the **abdomen massaged** if there is no contraindication. Mortimer (Lancet, June 17, 1911).

The administration of 15 grains (1 Gm.) of **chloretone** as a preliminary to anesthesia has been recommended to prevent post-operative vomiting as well as excitement during the induction.

To prevent nausea and vomiting after anesthesia, **chloretone**, in amounts from 5 to 36 grains (0.3 to 2.3 Gm.), given in a 5-grain (0.3 Gm.)

capsule, was used in 164 cases. The best results were obtained in adults with 10-grain (0.6 Gm.) doses given twenty to thirty minutes before starting the anesthetic. If it is given inside of twenty minutes the patient is liable to vomit soon after the anesthetic is started, thereby losing all benefit of the drug. While **chloretone** has not always proved a reliable specific in preventing nausea and vomiting, it has been a great aid. Vomiting, when present, usually took place before the return to consciousness. Beebe (Boston Med. and Surg. Jour., Oct. 6, 1904).

Before beginning the administration of the anesthetic the patient is given by the author 5 to 6 drops of a 5 per cent. solution of **alypin**, and this dose is repeated as soon as the patient is sufficiently recovered to swallow. This usually prevents all nausea, but if there is a tendency to it the dose may be again repeated in one or two hours. Wanietscheck (Prager med. Woch., Nu. 50, 1906).

To prevent vomiting, the author aims to oxidize the ether as soon as the anesthetic effects are no longer needed by the surgeon. This he accomplishes by administering **oxygen inhalations** immediately on suspension of the anesthetic, and continuing it until consciousness is regained, and in some cases even longer. He has used this method for two years in a variety of operations and always with success. W. T. Wootton (Jour. Amer. Med. Assoc., April 27, 1907).

Endorsement of McArthur's plan, which consists of giving 2 ounces (60 c.c.) of fresh **cold water to drink** after midnight on the morning of operation, repeating this every fourth hour until two hours before operation, when 10 ounces (300 c.c.) are given and repeated just before anesthetization begins. Gunn (Montreal Med. Jour., June, 1907).

Especially in the case of operations done during the first whiffs of ether, the **Bier constricting band**, applied to the **neck** immediately after the close

of the operation and left in place for a half to one hour, while the patient reclines, eliminates vomiting. Ritter (*Zentralbl. f. Chir.*, July 11, 1908).

The most rational way to treat and prevent nausea and vomiting after anesthesia is to promote elimination of the anesthetic. The patient should be kept **warm** so that the skin may act freely, and renal secretion should be helped by **saline enemata**, introduced slowly as soon as the patient is back in bed. While elimination is thus going on, the less put into the stomach the better. Thirst gives little trouble if enemata or subcutaneous injections are used. **Washing out the mouth with lemon-juice and water** is pleasant for the patient, and helps to allay thirst. J. Blumfeld (*Med. Press and Circular*, June 16, 1909).

The author urges that the patient drink an **abundance of water** for two days preceding the operation, and gives **saline enemas** every few hours after the operation to lessen the thirst, nausea, and shock. When not contraindicated by the operation, it is sometimes advisable, when ether mucus has been swallowed, to allow the patient to drink all the water desired as soon as consciousness returns; if this is vomited the stomach is washed out, and if it is retained the ether mucus is diluted. Another method, advocated by Kelly, is to **wash out the stomach** thoroughly after the operation, and then leave in it 6 ounces (180 c.c.) of a saturated solution of **magnesium sulphate**. L. F. Watson (*Old Dominion Jour. of Med. and Surg.*, Sept., 1909).

Thirty patients were given **olive oil** by mouth immediately after partial restoration of consciousness following an ether anesthesia. The results were striking. In certain of the cases nausea failed to occur at any time. In a second group in which nausea had begun prior to the administration of the oil it was immediately checked by it. In only 1 patient was nausea observed after

giving the oil. E. A. Graham (*Jour. Amer. Med. Assoc.*, Dec. 18, 1909).

The author administers 15 grains (1 Gm.) of **chloretone** in a capsule, one and a half hours before operating. It lessens the patient's dread; the anesthetic is taken more quietly and less is required; the patient comes out quietly (healing by first intention is thus facilitated, ligatures are less likely to slip, and bandages remain undisturbed), shock is markedly reduced, and nourishment can be taken freely as soon as the patient becomes fully conscious. The only drawback is that the drug may cause dizziness before the operation. L. W. Bickle (*Therap. Gaz.*, Mar., 1912).

**Respiratory Complications**, especially frequent after ether, occur in the form of bronchitis, lobular or lobar pneumonia, and edema of the lungs. They have been ascribed to irritation by the anesthetic, undue exposure of the patient to cold, and the inhalation of vomitus or septic fluids during the operation. Doubtless in many instances several of these causes have been simultaneously operative.

Acute edema of the lungs is one of the immediate sequels of ether narcosis, and, while comparatively rare, it must be reckoned with. In the case reported by the author the whole process appeared to have originated in the air-vesicles, and to have run its course and ended there. The most effective features in the treatment during the crisis were a large dose of **nitroglycerin**, moderate elevation of the foot of the bed, and very active **dry-cupping all over the chest**. The patient recovered. Any exposure during operation which tends to check active perspiration is very dangerous to both the lungs and kidneys. Pedersen (*Annals of Surg.*, Jan., 1906).

Study of 2500 cases of ether anesthesia, in nearly all cases with the Clover inhaler: 55, or 2.2 per cent., developed some lung complication;

32, or 1.28 per cent., came to autopsy; 35 occurred during the cold months of the year. The lung complications all developed within forty-eight hours; 37 cases had some septic focus before the development of the lung complications. In 8 cases the presence of emphysema was noted, in 1 there was chronic bronchial asthma, and in 9 cases chronic nephritis was present. There were 14 cases of lobar pneumonia, 16 of bronchopneumonia, 19 of bronchitis, 3 of plastic pleurisy. Armstrong (Brit. Med. Jour., May 19, 1906).

Lobar pneumonia following anesthesia differs from that commonly seen in lower and more irregular temperature, shorter and rarely a true crisis, greater freedom from complications, central type, lung signs developing late and cough not marked or severe, and sputum rarely blood tinged. In most cases more than one theory is necessary to explain the origin: 1. Irritant action of anesthetic; ether is the most irritant, chloroform the least. 2. Aspiration of mucus and vomitus and hypersecretion of mucus. 3. Emboli. 4. Toxic effect on heart and blood-vessels; chloroform is the most dangerous. 5. Presence of pneumococci and other bacteria in mouth and throat. 6. Extension of infection through subdiaphragmatic space. 7. Cooling of the body; a loss of temperature from a half to one degree may follow prolonged anesthesia without any other factor. 8. Limitation of lung expansion. 9. Lessened resistance of the patient. Prevention lies in disinfection of the mouth and nose as a routine measure, and administration of the anesthetic by the open drop method with the head low and to one side, and the jaw kept forward. The patients must be kept warm and dry by warm pads, jackets, and leg covers. Wight (Bull. Johns Hopkins Hosp., March, 1908).

Complications on the part of the lungs follow in about 5 per cent. of all laparotomies. A. Lăwen (Münch. med. Woch., Oct. 3, 1911).

Rovsing has proved experimentally that the bronchi are not at all irritated by ether, which, indeed, was originally used as an inhalation remedy for certain lung diseases. Mikulicz, substituting chloroform for ether, observed an increase of post-operative pneumonia, while local anesthesia caused a still greater increase. After abdominal operations the close relationship of the pleural to the abdominal lymphatics seems to explain its production. W. E. Darnell (Amer. Jour. of Obstet., Mar., 1917).

Such complications are particularly likely to occur, however, where predisposing conditions such as bronchitis, emphysema, old age, and general enfeeblement already exist.

Ether occasionally causes a latent tuberculous process to break out afresh.

The *treatment* of the respiratory complications is that classically recommended for the conditions present. The reader is referred to the articles on PNEUMONIA, BRONCHITIS, etc., for information in this direction.

**Renal Complications.**—Irritation of the kidneys, as shown by the appearance of albumin, casts and occasionally red blood-cells in the urine, may be observed after ether as well as after chloroform.

In 65 chloroform cases the urine showed albumin or casts (or both) induced or increased after inhalation in 40 per cent. of the cases, sugar occurring in 1 instance. In 61 cases of anesthesia produced by nitrous oxide followed by ether, albumin and casts occurred or were increased in the urine in 12 per cent., 1 case showing sugar. In 41 cases of chloroform followed by ether, albumin and casts were induced or increased in 41.5 per cent. of the cases. In 28 ether anesthetics, 39 per cent. of the cases showed albumin and



casts increased or present afresh after the narcosis, 2 cases also showing fresh occurrence of sugar in small quantities. Goodwin (Therap. Gaz., May, 1905).

Where renal disease already existed beforehand, suppression of urine may occur, and the condition of the kidneys be made worse.

The early effect of both ether and chloroform up to the period of complete insensibility is ordinarily an increase of the secretion of urine. This, as a rule, is more pronounced in the case of ether than of chloroform, but during full anesthesia, however prolonged, the secretion of urine is almost completely arrested. The depressing effect during this period is more pronounced with ether than with chloroform. On removal of the anesthetic the kidneys rapidly recover, and there is hyperacidity lasting for some hours. Thompson (Brit. Med. Jour., March 25, 1905).

During ether narcosis the volume of urine secreted is affected in two ways. In most instances there is a decrease, in a few an increase. The latter is probably an early or light effect, the former a pronounced effect. The maximum outflow of urine occurs about three hours after discontinuance of the anesthetic. With ether the urine when diminished in volume is, as a rule, more concentrated (contains more nitrogen). The converse is the case with chloroform. Arrest of urinary secretion occurs more readily and with a relatively higher blood-pressure in ether than in chloroform narcosis. The escape of leucocytes into the urine after full ether narcosis is more marked than with chloroform, probably indicating a higher degree of stasis in the glomerular capillaries. An increased excretion of chlorides is seen after ether inhalation, but much less and of shorter duration than in the case of chloroform. Thompson (Brit. Med. Jour., March 24, 1906).

The effect of chloroform and ether on the kidneys is merely one manifestation of a general intoxication of the

system from the drug. The old theory of a delayed toxic action on the kidneys has been sustained by recent research, which has revealed degeneration of the parenchymatous organs throughout, but most prominent in the kidneys. The least harmful of all techniques is general anesthesia with ether plus **oxygen**, preceded by an injection of **morphine**. Under all conditions the amount of the anesthetic used should be the smallest possible. Loss of blood should be combated in every possible way. The interval between successive anesthetics should be at least a week, and the second anesthesia should never be attempted until the urine is free from albumin and has lost its transient reducing power. M. Hirsch (Centralbl. f. d. Grenz. d. Med. u. Chr., Dec. 31, 1908).

The *treatment* of renal complications after ether comprises **saline enteroclysis**, the administration of **purgatives** and **irritating diuretics**, and other measures commonly employed in similar states otherwise arising.

**Late Poisoning.**—Disturbances of metabolism, due to persisting effects of the anesthetic upon the cells of parenchymatous organs, especially the liver, kidneys and heart, and culminating in acid intoxication, with marked restlessness, vomiting, delirium, convulsions and coma, sometimes followed by death, occur much more rarely after ether than after chloroform. The symptoms typically begin only a number of hours or two or three days after the anesthesia, and in fatal cases progress rapidly to a termination. This condition, with its treatment, has been fully discussed in the article on CHLOROFORM (Vol. III), to which the reader is referred.

In the fatal cases of late intoxication, death is almost invariably due to chloro-

form; ether is seldom the cause of a death of this kind. Bevan and Favill (Jour. Amer. Med. Assoc., Sept. 2, 1905).

Operations should be delayed when possible if a fatty liver be suspected, *e.g.*, in subjects of rickets and infantile paralysis who have been overfed with fattening food and underexercised; in cases of sepsis and diabetes, and when a history of cyclic vomiting is obtained. When a child has recently vomited apparently without cause, an intended operation should be postponed. When fatty liver is suspected the patient should be kept for some days on a diet restricted in fat. **Bicarbonate or citrate of soda** should be given. Mild purgation may be beneficial. Starvation will cause acute acetonuria; therefore nutrient enemata should be given two hours before and immediately after an operation. The treatment of acid intoxication following operations should be by **venesection, saline transfusion, and clysters of solution of bicarbonate of sodium**. L. G. Guthrie (Clinical Journal, June 12, 1907).

The old treatment of postanesthetic acidosis was to give alkalies, but that line of action no longer appears convincing. The disease is due to exhaustion of the liver and to damaged tissue, and the treatment is to give **glucose**, if possible by the mouth, or, failing this, by rectal injection; treated in this way, these cases do, as a rule, extremely well. Buxton (Clin. Jour., April 24, 1912).

**Postanesthetic Paralysis.**—This is a complication only indirectly due to the anesthesia, and consisting in loss of function of certain nerves due to pressure upon them by reason of faulty positions of the patient during operation or to the resting of limbs on the edge of the table. The most common paralysis occurs in the arm, and is due to pressure exerted upon the musculospiral nerve as the arm hung down beyond the table-margin. The brachial plexus may

also be affected, owing to pressure from the head of the humerus in a case where the upper extremities have been kept above the head during the operation.

Postoperative paralysis results from temporary pressure of the head of the humerus on the infraclavicular portion of the plexus, due to hyper-elevation of the arm, with rotation inward. The author favors Holst's method of securing the arms at the sides, resting on cushions. Glitsch (Zentralbl. f. Gynäk., Nu. 39, 1904).

Paralysis of nerves of the leg or face also occasionally occurs. The paralysis is not generally permanent.

In rare instances, more widespread paralysis follows operation, owing to cerebral hemorrhage or embolism resulting from the primary stimulating effect of ether on the circulation.

Anesthesia paralysis occurs in two forms, peripheral and central. The peripheral may be averted by proper treatment during narcosis. The central cannot be prevented, though its danger may be avoided by limiting the quantity of anesthetic and by a preliminary hypodermic of **morphine** in ether anesthesia or ether narcosis, to control excitement. Halstead (Wisc. Med. Jour., Feb., 1908).

**ANESTHESIA BY INTUBATION AND INTRATRACHEAL INSUFFLATION.**—In cases where anesthesia with the mask is difficult and where it is earnestly desired to use as little of the anesthetic as possible, Kuhn introduced a method consisting in intubation of the larynx and connection of the intubation tube with a rubber tube attached to a funnel covered with gauze, on which the anesthetic is dropped. By this procedure there is gained absolute control of the amount of anesthetic administered, and relief from the risk

of swallowing blood as well as from the necessity of frequently interrupting anesthesia in facial, nasal, and buccal operations.

In 1909 Meltzer and Auer discovered a new method of effecting artificial respiration which later on proved in addition highly advantageous, under certain circumstances, for the administration of anesthetics. The principal feature is that, by means of a tube passed into and fitting loosely the trachea, ether-laden air is led in a nearly constant stream approximately to the tracheal bifurcation. So perfect an artificial ventilation of the lungs is thus secured that the respiratory movements become largely or wholly unnecessary, and correspondingly cease. Either or both sides of the thorax can now be entered for surgical procedures without any ill-effects from the resulting pneumothorax. The diminished number of respiratory movements furthermore, facilitates the performance of such procedures. A very complete aëration of the intrapulmonary surfaces is insured by this method, and the patients therefore recover quickly from the anesthetic.

The apparatus required, in its simplest form, consists merely of a foot-bellows, a Wolff bottle, a mercury manometer, and a soft-rubber catheter. These are united by rubber tubing so that air can be forced through ether in the Wolff bottle and thence through the catheter into the lungs, while the pressure of the air-current is constantly indicated by the mercury manometer.

The apparatus described consists of a Wolff bottle with three necks placed within a copper water-jacket, and a foot-bellows. By means of

cocks the stream of air can be carried through the hot water, over the top of the ether in the Wolff bottle, or through the ether when a particularly strong vapor is desired. Air and ether vapor may be mixed in any proportion. Connected with the delivery end of the apparatus is a safety valve and pressure regulator consisting of a bottle of mercury into which a tube is plunged. The depth of the tube in the mercury, which is adjustable, represents the maximum of pressure which is allowed within the apparatus; if for any reason the pressure should rise, the valve "blows off" automatically.

The air or mixture is supplied at a practically constant temperature of about 10 degrees above room temperature. As an intratracheal tube the author uses a French lister catheter, 22 to 24 F., moistened in hot water to render it pliable, a new and sterile one being used for each case. For the introduction of the tube, he uses a laryngeal forceps with sleeves attached for grasping the tube near its extremity. Ehrenfried (*Boston Med. and Surg. Jour.*, April 13, 1911).

Case in which extensive subcutaneous emphysema followed intratracheal anesthesia. Second accident in New York City; the first was fatal, showing method is not without danger, and that a safety valve (so that the pressure cannot exceed 15 mm. Hg.) is absolutely essential. The following may occur: direct trauma due to the catheter, either during introduction or afterward, or from pressure of the sand bags under the neck; trauma by overdistension, by inserting catheter too far, and thereby tightly plugging a bronchus, leading to rupture of the lung; obstruction from extreme flexion of head and pressure of the sand bags under the neck; the catheter may be too large. H. C. Luke (*Surg., Gynec. and Obstet.*, Feb., 1913).

By means of intratracheal insufflation one of the dangerous effects of ether and chloroform is eliminated, that resulting from partial or

complete respiratory paralysis, for the respiration is produced artificially. It does not necessarily cause apnea, for spontaneous respiratory movements may still be detected. When the dose of ether is too large, the first sign is the cessation of the spontaneous respiration—a danger signal that the etherization has entered the toxic zone, and since it may be hours before the real danger appears, it is a safe and valuable signal. The results with chloroform are different; when the anesthetic dose is excessive, respiration and blood-pressure go down practically together, and in a comparatively short time. Githens and Meltzer (*Jour. Amer. Med. Assoc.*, Apr. 26, 1913).

Since the introduction of intratracheal anesthesia in 1909, it has been employed successfully in the Johns Hopkins clinic, in all types of cases, but chiefly in operations about the head and neck and in the thorax and spinal canal. Pure air is brought directly into the larger bronchi, while the vitiated air is forced out by the returning air streams, and the dead space of the mouth, pharynx, larynx and trachea is eliminated. The anesthetist has been relieved almost entirely from the embarrassment due to cyanosis. The difference in the effect on the pulse is marked. With intratracheal anesthesia the average increase was 27 beats as against 47 with drop ether. Watts (*Jour. Amer. Med. Assoc.*, Sept 4, 1915).

In all 3 forms of insufflation, the tracheal, the pharyngeal, and the buccal, there are common advantages over the usual inhalation methods. These advantages are that the vapor is warmed before delivery to the patient, and the rate of administration can be more evenly maintained, with consequent smoother anesthesia and a lessened liability to overanesthesia. In the tracheal and pharyngeal insufflation the obstruction at the base of the tongue is automatically removed, and therefore there is no de-vitalization of the patient by forced breathing. The insufflation method is

especially indicated in operations upon the throat and the chest. R. C. Coburn (*Med. Rec.*, Mar. 3, 1917).

In intratracheal anesthesia the diversion of a portion of the air stream over the ether surface has usually been accomplished by means of stop-cocks in the tubing. The writer describes a new "constant volume valve" which constitutes essentially a convenient means of regulating all these (3) stop-cocks synchronously. The mixture of ether vapor from a Wolff bottle with air may thus be adjusted in any proportion without changing the volume or pressure at which the mixture is delivered. Gates (*Jour. of Exper. Med.*, July, 1917).

Intratracheal insufflation was used by the writer in 930 cases. In 407 of these it was used for operations on the face, mouth, and pharynx in which there was bleeding into the air passages. When difficulty is experienced in exposing the vocal cords the application of a 5 per cent. solution of cocaine to the pharynx and epiglottis is recommended. This is particularly helpful when light anesthesia is indicated and refutes the criticism that the depth of anesthesia necessary to pass the catheter prohibits the application of the method in cases of this kind, in which its use is especially advantageous. F. E. Shipways (*Proc. Roy. Soc. Med.*, London, xiii, Sect. Anes. 1, 1919).

The technique of the insufflation anesthesia is as follows: The patient having first been anesthetized in the ordinary way, a 10 per cent. cocaine solution is sprayed over the pharynx. With the head extended over the end of the table, and the tongue pulled forward, the glottis is held open with the forefinger of the left hand, while the right passes into the trachea a catheter having a diameter about one-third that of the canal. Too large a catheter causes shallow breathing and cyanosis under small pressure, whereas one too small fails

to keep the patient under. For the average adult a catheter No. 22 to 28 French is suitable. It is passed down to within one inch of the bifurcation, which measures on the catheter about 26 cm. from its tip.

Description of an introducer for the tracheal tube, following nearly in curve and angle the O'Dwyer apparatus. When the patient is etherized fully with inhaler or cone, a mouth-gag is inserted on the patient's left, the tongue dragged forward sharply with tongue forceps, the operator's left index finger thrust down until it meets the epiglottis, and the introducer, held in the right hand, is pushed in and down, alongside the left forefinger, till it has passed the upper projecting edge of the epiglottis. Then the heel of the instrument is pitched upward, and the assistant feeds the catheter into the larynx and trachea. At first nitrous oxide was given with the usual oxygen coefficient till consciousness was lost, and anesthesia then deepened by the addition of ether till the laryngeal reflex was abolished, when the intratracheal tube was introduced. Cotton and Boothby (*Surg., Gynec., and Obstet.*, vol. xiii, p. 572, 1911).

Two methods of introduction of the tube have been in use—that of direct inspection through a Chevalier-Jackson laryngoscope; and by means of a specially constructed introducer in which the tube is threaded through a tunnelled urethral sound with an O'Dwyer curve to hook over the arch of the tongue. The tube should be 22 F. for most adults, occasionally 24 in thoracic cases, to insure a return flow of air not too great for the maintenance of sufficient intrapulmonary pressure. If the tube is so small as not to provide for sufficient pressure to keep the lung inflated when the chest is open, according to Meltzer pressure just below the thyroid notch, at the middle of the thyroid cartilage, every few minutes will remedy the defect. Woolsey

(*N. Y. State Jour. of Med.*, April, 1912).

The bellows are then attached and a mixture of air and ether pumped in a steady stream into the trachea under a pressure of about 12 mm. of mercury. The catheter, by partially obstructing the outflow of air and ether, raises the intrathoracic pressure. When the thorax is open the lungs may be collapsed or distended at will by decreasing or increasing the pressure. The respiration becomes shallower as the pressure is raised (H. H. Kerr).

Elsberg has devised and uses an electrically driven, improved form of the apparatus above referred to, while H. H. Janeway still more recently has described a further improvement and elaboration (Fig. 7) of the original mechanism, which is so planned as to supply a current of warmed, moistened and filtered air, containing any desired amount of ether vapor, and interrupted at regular intervals. The interruptions in the flow are very important in that they not only assist the diffusion of oxygen in the lungs, but overcome the tendency to obstruction of the venous return flow to the heart resulting from the pressure of the constantly distended lung on the great veins. Janeway's apparatus is also provided with a blow-off safety-valve, to guard against injury to the patient's lung if an accidental marked rise of pressure should take place owing to faulty introduction of the tracheal tube. Foot-bellows are always to be kept at hand for use in case the electric current actuating the motor should happen to give out.

From the moment the power is turned on and the pressure regulated,

the anesthetist has nothing to do but watch the pressure gauge and occasionally interrupt the current of air so as momentarily to collapse the lungs. The tracheal tube must be fairly rigid so that it cannot be coughed out when once in place. This requirement is best met by a silk-woven catheter. It should have an opening at or near its end and must be at least 30 cm. long. The ordinary silkworm urethral catheter will do very well, and has the advantage that it can be obtained anywhere. The catheter should have two marks upon it, one 12 cm. from the tip, and a second 26 cm. from the tip. Therefore, if the tip of the intratracheal tube is 26 cm. from the incisor teeth, it will lie 5 cm. or less above the bifurcation of the trachea. For the adult it is advisable to use a tube whose diameter measures about one-half of the length of the glottis as seen through a direct laryngoscope. The author insufflates pure air for a few minutes at the end of the anesthesia so as to blow out the anesthetic from the lungs and trachea. So quickly will the patient react that one must be careful that he is receiving enough ether mixed with the air during the operation. C. A. Elsberg (*Annals of Surg.*, Feb., 1911).

From observations in 216 cases the author regards insufflation anesthesia as safe if certain cardinal principles are observed in its administration, viz., one must guard against overpressure, spraying of liquid ether through the tube, introduction of the tube into the esophagus, introduction of the tube beyond the bifurcation of the trachea, and trauma to the pharynx or larynx in intubation. Proper apparatus and ordinary caution should absolutely prevent the accidents responsible for the few deaths reported from the method. The uniformly sufficient aëration of the lungs, with the even administration of well-diluted ether vapor, relieves the respiratory apparatus and central nervous system of much

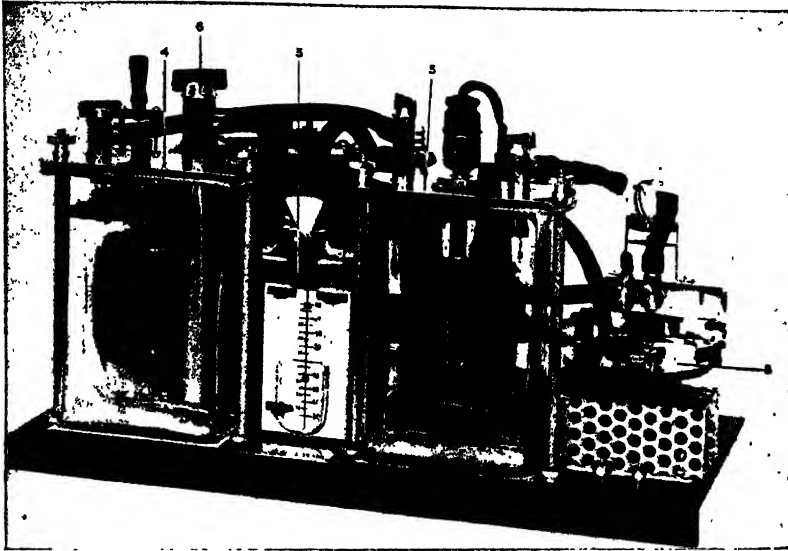
strain, and overetherization is impossible. Peck (*Annals of Surg.*, July, 1912).

Endotracheal insufflation anesthesia, properly administered and safeguarded, can be rendered devoid of intrinsic danger. It is indicated whenever the operation is about to interfere in any way with the ability of the patient voluntarily to respire. Of the various anesthetics to be used with this method, ether with air is the most applicable for general use; however, **nitrous oxide oxygen** with minimal quantities of ether may occasionally be the anesthetic of choice. To prevent deaths from emphysema, the apparatus must be provided with a safety-valve by which the endothoracic pressure cannot exceed 15 mm. Hg. Cotton and Boothby (*Annals of Surg.*, Jan., 1913).

Woolsey enumerates the indications for intratracheal anesthesia as follows: (1) Intrathoracic surgical cases where its positive intrapulmonary pressure presents acute pneumothorax. (2) That class of cases where the obstruction to breathing exists in the air-ways between the teeth and the trachea, from collapsed *alæ nasi*, recedent jaw and tongue, or paralyzed soft palate and glottis, and in which narcosis is generally maintained in spite of serious anoxemia. (3) In cases where the factor of safety is lowered by age or disease. (4) In all operations of serious nature about the oral or nasal cavities, where aspiration of blood and tumor material would be a source of danger.

Report of a case in which operation was undertaken for a **large sarcoma beneath the clavicle**. Under ether narcosis a catheter was easily introduced into the glottis. Laughing gas and ether anesthesia was continued through the catheter. The operation lasted about an hour and only 100 gr.

A



B

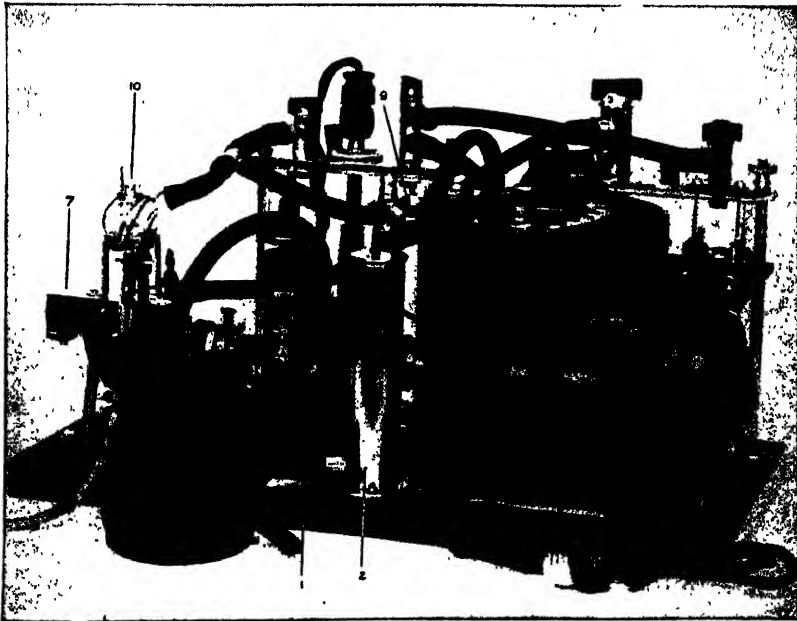


Fig. 7.—Janeway's apparatus for intratracheal insufflation. *A*, front view. 3, valve for regulating the amount of air passed over the surface of the ether; 4, ether jar; 5, water jar; 6, valve for bubbling a portion of the air through the top layers of the ether; 8, worm wheel operating interrupting valve. *B*, back view. 1, blower; 2, air filter and muffler; 7, interrupting valve; 9, safety-valve controlling the pressure; 10, condensing bulb.

(Annals of Surgery.)

of ether were required. The patient's condition remained good throughout the operation and a necessary incision of the pleura was borne without the slightest disturbance. E. Unger (Berl. klin. Woch., Sept. 19, 1910).

Intratracheal insufflation anesthesia found very useful in **operations on the neck**, such as **thyroidectomy**. The operator can manipulate the trachea as much as necessary without causing disturbance in breathing or interfering with the anesthesia. Nor need he fear a sudden collapse of the trachea during the removal of a large **goiter**. The method is of great value in operations on the tongue and mouth and in operations on the superior and inferior maxilla, in which the buccal cavity or pharynx has to be widely opened. There is no danger of aspiration of blood into the lungs, and tamponade of the larynx is unnecessary. The current of air continually flowing upward in the trachea by the side of the tube will blow out all blood tending to run down into the larynx and trachea. The anesthesia should be advantageous in **operations on the brain** and the **spinal cord**, such as bilateral suboccipital **craniotomy** and **laminectomy**, in which the patient has to be in the prone position. Elsberg (Annals of Surg., June, 1911).

Tracheal insufflation anesthesia offers the best available conditions for progress in surgery of the **thoracic cavity**. Nitrous oxide and oxygen can be successfully exhibited through the intratracheal tube. Unfavorable results that have been reported have had their origin in easily remedied faults of technique. Use no force in the introduction of the tracheal tube. Use only the lowest concentration of ether compatible with narcosis. Never insufflate without an efficient and suitable mercury manometer and safety-valve that will register a maximum of 20 mm. of mercury. W. C. Woolsey (N. Y. State Jour. of Med., April, 1912).

Report of 2 cases in which Meltzer's method of intratracheal insuffla-

tion was applied, proving in one a direct life-saving measure. This was an operation for **sarcoma of the nasopharynx**, orbit, and **maxillary sinus** which had twice recurred after removal. The first symptoms had been noted eight months before. With the intratracheal Meltzer technique the operation was conducted safely and more radically than had previously been possible. R. Alessandri (Polí-clínico, Sept. 8, 1912).

Intratracheal insufflation anesthesia used in almost 500 cases of all kinds. Outside of its special field, **thoracic surgery**, the author has found it of great value in cases of **intestinal obstruction**, for it completely does away with the dangers of aspiration of vomited matter. It seems particularly well borne by very weak and cachectic patients. In **goiter** operations it prevents cough and tracheal collapse. In those patients with a **chronic bronchitis** or some pulmonary trouble, it seems entirely to do away with the danger of subsequent pneumonia. Elsberg (N. Y. State Jour. of Med., Sept., 1912).

Some of the advantages of the intratracheal procedure in ordinary anesthesia are as follows: Prolonged anesthesia appears to be harmless; there is no rattling of mucus in the throat; cough and lung complications are not produced, and postoperative vomiting is absent.

In all but a few of 200 cases, the anesthesia was very satisfactory, and it was particularly free from complications and after-effects. Elsberg (Annals of Surg., Dec., 1911).

Intratracheal insufflation anesthesia employed in 25 cases. The patients recovered more quickly, the after-effects were lessened, vomiting was only noticed once, and from the surgeon's point of view the **anesthesia** was perfect. The anesthetist has a greater sense of security, for if at any time he thinks that artificial respiration may be necessary, he has the apparatus ready at hand and has



merely to turn the pointer from "ether" to "air." R. E. Kelly (Brit. Med. Jour., July 20, 1912).

**General Analgesia by Oral Administration.**—This method is used for minor but painful procedures so frequently necessary in connection with wholesale war surgery, and especially painful dressings. It does not necessitate the removal of the patient from the bed and does not result in subsequent nausea and vomiting. It is especially useful when large numbers of such dressings are a necessary daily routine.

After a series of animal experiments to determine the feasibility of producing general analgesia by the oral administration of various narcotic drugs, the following mixture was tried by the writer on man with favorable results:—

*Ether*,  
*Liquid petrolatum*, of  
each . . . . . 16.0 (4 drams).  
*Peppermint water* . . . . . 0.3 (5 minims).

This dose could be taken with ease and very little bad taste if sandwiched between mouthfuls of port wine. It produced a marked degree of general analgesia, sufficient to permit otherwise painful dressings being accomplished without discomfort. Combined with a few whiffs of chloroform, short operations could also be performed without pain. The formula was improved, and as now used is: **Chloroform**, from 2 to 4 Gm. ( $\frac{1}{2}$  to 1 dram) and 14 Gm. ( $3\frac{1}{2}$  drams) each of **ether** and **liquid petrolatum**. The solution produces no ill after-effects, and is quite without danger, as it does not produce anesthesia. The vaporization of the ether has been shown to be slow and uniform from oily solution, hence the action of the mixture is even and continued. Gwathmey and Karsner (Jour. Amer. Med. Assoc., Apr. 6, 1918).

## INTRAVENOUS ANESTHESIA.

—In 1909 Burkhardt advanced the view that it is unnecessary for an anesthetic to pass through various tissues before entering the blood, and that the most direct and satisfactory method of anesthesia is to introduce the drug directly in the blood-stream. In his first trials with ether in 33 human cases, a 5 per cent. solution of the drug in normal saline solution was used. No cardiac or respiratory disturbances were observed, and almost no after-effects—such as headache and vomiting—were met with. No abnormality of the urine, and no thrombosis or other bad result, were noted.

In 4 of the 33 cases, however, it was not found possible to secure complete abolition of the reflexes. The amount of fluid injected ranged from 200 to 800 c.c. Recovery from anesthesia was rapid. Morphine and scopolamine were generally injected before the intravenous anesthesia.

Children require 10 to 17.5 c.c. ( $2\frac{1}{2}$  to  $4\frac{1}{2}$  drams) of 5 per cent. ether for complete anesthesia; women 10 to 30 c.c. ( $2\frac{1}{2}$  to  $7\frac{1}{2}$  drams), and men 10 to 40 c.c. ( $2\frac{1}{2}$  to 10 drams). As soon as the reflexes begin to return, it is only necessary to open the cannula and allow 30 to 70 c.c. ( $7\frac{1}{2}$  to  $17\frac{1}{2}$  drams) more of the solution to flow into the vein. Narcosis is complete in eight to ten minutes, and the stage of excitement is usually very short. All the disagreeable by-effects of ether anesthesia, such as cyanosis and disturbances of respiration, rattling in the throat, etc., are absent. The author highly recommends intravenous anesthesia in affections of the cardiac and respiratory organs, and in feeble and debilitated individuals. It is also excellent in operations about the head and neck. L. Burkhardt (Münch. med. Woch., Nov. 16, 1909).

Since in inhalation anesthesia the anesthetic is absorbed from the vapor introduced in the air-passages, the dose actually entering the blood is variable, being subject to all the accidents of laryngeal spasm, respiratory spasm, and variations in the depth of respiration. The exposure of the respiratory tract to an irritating vapor is a serious drawback. The absorption of the drug by the patient cannot be stopped abruptly, but must go on until the patient has rid himself of the vapor which fills his lungs and of the anesthetic-sodden mucus in his bronchial tubes and stomach. In operations on the mouth, jaws, or pharynx the labors of the surgeon are made much harder by his having to share the field of operation with the anesthetist. By direct administration of an anesthetic by the blood all these difficulties are disposed of. The author has given ether infusion anesthesia in 136 cases, using a 5 per cent. solution in **normal saline** and an apparatus provided with an indicator. The introduction of the cannula must be carried out with the strictest aseptic precautions. Induction of anesthesia is usually quite smooth and rapid, three or four minutes on the average. The chief features of the anesthesia are regularity and smoothness, the ease with which it can be graduated, and the great rapidity of response to slight alterations in dose. Of the 136 patients, only 6 vomited and of these 3 had swallowed blood during the operation. The advantages were most striking in extreme inanition. F. Rood (Proc. Royal Soc. of Med., April, 1912).

From experience in 170 instances of intravenous ether narcosis the writer regards it as an ideal form of narcosis and thinks it is to be regretted that it is so little used. He believes the injuries observed in certain quarters must be due to faulty technic. It is remarkable how quietly the patients "go under," how calm and pleasant the course of the anesthesia is, and how fresh the patients look when they come out of it. However, the method is adapted only for the clinic, not for

general practice. Momburg (Deut. med. Woch., Oct. 13, 1921).

Since that time other surgeons have taken the method up, using not only ether, but various other drugs, sometimes in conjunction with the ether. The procedure now most generally followed is that of Rood: A 5 per cent. solution of ether in filtered normal saline solution flows from a 2-liter reservoir, adjusted on a stand eight feet above the floor, through an indicator (in which the amount of solution being used at any given time can be observed), then through a warming chamber into a blunt cannula and so into the vein. The indicator consists of a cylindrical or globular glass bulb of a capacity of 2 to 4 ounces with an inside pipette, very much as in Murphy's apparatus for proctoclysis. When the apparatus is working properly, the lower half only of the indicator is filled with solution. The solution flows from the tank through the pipette and drops on the surface of the fluid in the lower half of the indicator. By means of a compression tap below the indicator, the rate of flow is accurately controlled. The patient's arm is bound to a padded splint, the bend of the elbow wiped with a 5 per cent. solution of thymol in carbon tetrachloride, and the skin anesthetized with 1.5 per cent. cocaine, the median basilic exposed through a small incision, and a small blunt cannula inserted. The ether solution is at first administered at full flow, then reduced at the appearance of the usual signs of surgical anesthesia—in from one to five minutes. The solution now drips in a very fine stream or at the rate of 40 to 60 drops a minute, the corneal reflex afford-

ing a reliable guide for administration. The customary attention should be paid to maintaining an open airway for respiration, and furthermore, as in inhalation anesthesia, economy in the amount of ether solution administered is of paramount importance. The infused fluid must be kept at a temperature not higher than 90° F., otherwise the ether volatilizes and escapes.

The best temperature for infusing the ether solution intravenously is 38° C. (100.4° F.). Ether is soluble at this temperature only to the extent of 4.68 per cent. With lower temperature more ether will dissolve, and there is always danger of hemoglobinuria with more concentrated solutions. The advantages of intravenous ether narcosis are especially apparent in operations on the face and in cachectic patients. Loss of blood is better tolerated, the pulse remains stronger, and the patients do not complain so much of thirst after the operation. R. Hageman (Münch. med. Woch., July 11, 1911).

Experience with intravenous narcosis in 250 cases. The author employed, in connection with ether, a variety of hypnotics, including urethane, hedonal, chloral hydrate, isopral, chloralamide, veronal, and veronal-sodium. He regards ether in combination with **isopral** as the most effective method of intravenous anesthesia. These agents are separately infused. At first a 1.5 per cent. solution of isopral is instilled in amounts of about 40 c.c. (10 drams) to the minute, the total amount introduced ranging from 100 to 200 c.c. (3½ to 6¾ ounces). This is followed by the ether. Intravenous anesthesia is contraindicated in cases of myocardial degeneration, severe arteriosclerosis, nephritis, marked icterus, cholemia, general congestion and plethora. On the other hand, it is particularly indicated in conditions of collapse, profuse loss of blood, cachexia, debility, disturbances of the respiratory organs and peritonitis, as well as in **operations on the head and neck**, including the

buccal and pharyngeal cavities. L. Burkhardt (Munch. med. Woch., Nov. 15, 1911).

Intravenous anesthesia is indicated in operations about the head and neck, in hemorrhage, in weak cachectic patients, in diseases of the respiratory tract where inhalation anesthesia is objectionable, etc. It is contraindicated in nephritis, extreme arteriosclerosis, severe heart lesions, plethoric patients, etc. In the author's opinion, its chief field of usefulness will be found in **operations about the neck**. Dodge (Boston Med. and Surg. Jour., Dec. 28, 1911).

A total of 498 cases of intravenous ether anesthesia are now on record, with 2 deaths, 1 of unknown cause and the other a case of embolism reported by the author, while Kuttner has reported a case of clinically diagnosed embolism. The author thinks there can be no doubt that the fatality in his case was the result of the infusion, but whether the ether was responsible for it or the salt-solution vehicle was not absolutely certain. He infused 810 c.c. (27 ounces) of normal salt solution containing 5 per cent. of ether. Löfberg (Hospitalstidende, May 8, 1912).

The intravenous ether method is especially useful in **operations on the head, throat, and neck**, as the anesthetist does not encroach on the field of operation. It answers well in cachectic patients generally, and may be employed with advantage in collapsed abdominal cases and in operations attended by surgical shock, such as those for **ruptured ectopic gestation**, **Wertheim's operation**, **removal of the breast**, etc.—that is, in cases where saline transfusion is beneficial. In a case of the author's in which **ileosigmoidostomy** was performed there was absolutely no vomiting after the operation, although there had been a great deal of necessary manipulation of the intestine.

The procedure is contraindicated in the alcoholic, plethoric, and muscular type of patient, in cases where there

are advanced changes in the vascular and pulmonary systems, and in all cases in which transfusion would increase backward pressure on the right side of the heart.

The advantages over inhalation anesthesia in selected cases are: The patient is spared the disagreeable sensations; there is no primary irritation of the respiratory organs or of the heart; a very small amount of anesthetic is used; anesthesia, when produced, is of a calm and placid nature; there are no after-effects; headache and vomiting practically never occur, and pulmonary complications are absent. F. L. Napier (*Glasgow Med. Jour.*, July, 1912).

Report of 26 cases of ether anesthesia, using Burkhardt's method of a continuous flow into a vein of a 5 per cent. ether solution, alternating with a **normal salt solution**. The anesthesia was prompt and in every way satisfactory, with no untoward effects. Vostifeeva (*Roussky Vrach*, Sept. 8, 1912).

The author describes an apparatus for **intravenous ether anesthesia** in which the temperature of the solution is easily regulated by means of an electric bulb, all gas-bubbles are isolated from the solution before entering the vein, and all danger of infection is avoided. Cold, sterile, physiological **salt solution** is filtered through sterile filter-paper into a sterilized bottle up to a graduated mark at 2325 c.c. (2 $\frac{1}{4}$  quarts) and 175 c.c. (5 $\frac{3}{4}$  ounces) of ether is then added, making 2500 c.c. (2 $\frac{1}{2}$  quarts). After being heated in a copper coil, the solution passes through a "gas separator" and reascends to the original container, whence it is drawn off by a short tube into the vein.

The average requirement for an operation lasting one or two hours is 1 to 1 $\frac{1}{2}$  liters (quarts) of the ether-salt solution, and 2 liters have been given with absolutely no untoward effects.

The patient goes to sleep on 250 to 500 c.c. ( $\frac{1}{2}$  to 1 pint) in from eight to ten minutes. As soon as complete relaxation is obtained the solution may be kept shut off over half the time. When the patient shows signs of restlessness,

about 25 c.c. (6 drams) of solution gives a very prompt response. This advantage over the inhalation method is due to the fact that the latter depends for its efficiency upon the patient's respiration, which is inhibited at this stage (when the patient is coming out). Respiration is quiet. The pulse is increased, as during ether inhalation, but apparently not so much. The blood-pressure, taken at ten-minute intervals, does not show a rise in proportion to the amount of liquid injected.

The following objections to the method might be raised: (1) Infection. Any careful operator should be able to eliminate this. (2) Embolism. Gas embolism is prevented by the use of the separating device, and the possibility of volatilization after entering the blood-vessels is reduced by the admixture of unsaturated blood-plasma, thus reducing the vapor tension. Blood-clot embolism from clotting of blood in the cannula when solution is not flowing may be obviated by a little care in washing out the cannula occasionally. (3) Overfilling of the circulatory system. The author's observations did not show any marked increase of intravascular pressure. (4) Hemolysis. No hemoglobinuria was observed and blood examinations did not reveal laking of the erythrocytes.

The series of cases operated by the author included the following major operations: Extensive **repair of male perineum**, **decompression**, **panhysterectomy**, **epithelioma of the lip** with plastic work, **brain tumor**, and **hernia**. L. W. Jenkins (*Northwest Med.*, Dec., 1912).

Advantages of intravenous general anesthesia emphasized. The preliminary stage of excitement is nearly always absent, the respiration is almost natural, the color of the skin remains good, and the relaxation and flexibility are entirely satisfactory to the operator. The degree of narcosis can be maintained exactly, and when the operation is finished the patient is almost if not quite rational. The anesthetics used by the authors are varied: a 5 per cent. solution of ether, with filtered,

sterile, normal saline solution at 85° F. (29.4° C.); **hedonal** dissolved in normal saline solution at 70° F. (21.1° C.) to make a 0.75 per cent. solution; **paraldehyde**, 2.5 per cent., and ether, 3 per cent. in normal saline solution; or paraldehyde alone. Ether always raised the blood-pressure 2 to 20 mm., while with **hedonal** it fell 10 to 12 mm. One case purposely selected, with a blood-pressure of 186 mm. dropped to 142 mm., and remained at that level for some hours. There were no evidences of hemolysis beyond that usually occurring in ordinary saline transfusion, or in the respiratory administration of ether. As far as the blood-picture is concerned, **hedonal** is well borne. Complete anesthesia occurs in from one and one-half to twenty-three minutes with ether; with **hedonal**, in from twelve seconds to four minutes. Honan and Hassler (Med. Record, Feb. 8, 1913).

The intravenous method was employed by Ore as early as 1872, who used **chloral hydrate** in 51 cases, with considerable success. A number of fatalities discouraged its employment. Burckhardt, in 1909, tried anesthesia intravenously on the human subject, after experiments on the lower animals. **Chloroform** was first used, but abandoned for **ether**, deemed much safer. One year later 6 surgeons at the Berlin Surgical Congress corroborated the work of Burckhardt. The method was first used in America in 1912 by Honan, of the Metropolitan Hospital, New York City. In February, 1913, Honan reported 78 cases. The intravenous method has been employed in over 300 cases at the Metropolitan Hospital and elsewhere. Federoff collected 500 cases from 3 Russian clinics, in which **hedonal** 75 per cent. in normal saline was used, without deaths which could be ascribed to the anesthetic.

The objection to the use of **hedonal** is that a large number of red blood-corpuscles undergo hemolysis, while **paraldehyde** increases blood-pressure beyond the limits of safety. The

writer advocates the use of **isopral** and **ether** 7 per cent. in normal saline solution. **Isopral** (trichlorisopropyl alcohol) is a white crystalline substance closely related to **chloral hydrate**, and lowers blood-pressure. Candler (Jour. Mich. State Med. Soc., June, 1914).

At the end of the operation, unless it has been very long, the dressing should be applied before the flow of ether is stopped, as the return to consciousness often comes very promptly (Honan and Hassler).

**RECTAL ANESTHESIA.**—Pirogoff called attention to this method of anesthesia in 1847. In 1884 Mollière took it up again. Finally, in 1904, Krougiline used it in 43 patients, and since that time greater interest in it has been awakened. It seems to possess inherent disadvantages, however, such as difficulty of management, tendency to irritate the rectal mucous membranes, and the possibility of death through rupture of a previously unrecognized intestinal ulcer, which will probably preclude its frequent use. Gwathmey's special procedure of ether-oil colonic anesthesia has already received consideration in this article. (See page 654).

The advantages of rectal etherization are so great in operations on the face, mouth, neck and thorax that it deserves the preference in these cases. Irritation of the bowel can be avoided by blending the ether with **oxygen**, at body temperature, and preceding the application by a brief inhalation of **ethyl bromide** to relax the ileocecal valve. With this technique, general anesthesia by rectum is no more dangerous than by inhalation, unless the intestines are diseased. The author uses a Y-tube, one branch conveying the oxygen alone, the other branch passing it through a flask of ether, and the two

branches then uniting in a single tube which conveys the mixture into the bowel. The oxygen and ether are rapidly absorbed and there is no meteorism as when air is insufflated. The anesthetic vapor should be introduced slowly. When the operation is completed, the rectal tube should be disconnected and as much as possible of the ether expelled with the aid of abdominal massage. Rectal narcosis has some contraindications—bad or doubtful conditions of the intestine, acute or chronic affections of the abdomen, operations upon the perineum or genital organs. It is not superior to the other methods in operations on the extremities, but does offer advantages in **operations on the face, neck, mouth, and upon the thorax.** It is a method to be used only exceptionally. Leguen, Morel and Verliac (*Arch. gén. de chir.*, July 25, 1909).

Description of an apparatus for rectal anesthesia consisting of an outer jar (a galvanic cell) containing an ether bottle, the intervening space being filled with water at 90° F. (32.2° C.). Through the rubber cork is passed a long glass tube connecting with an ordinary cauterizing bulb, while a second perforation in the cork is occupied by a short tube providing for the exit of ether vapor. Between the bottle and the rectal tube is introduced a T-tube for the rapid relief of tension within the bowel or the attachment of an oxygen supply. Eberts (*Montreal Med. Jour.*, Feb., 1910).

The colonic method of administering ether is more complex than the pulmonary method in general and requires from the anesthetist a broader appreciation of the physiological factors involved. It is a valuable addition to the armamentarium of the trained anesthetist. The indications are: **Operations on or about the respiratory tract, especially such as lay open the mouth, larynx, pharynx, and trachea;** when ether absorption must be minimized on account of lung, heart or kidney lesions; respiratory embarrassment. The contraindications are lesions of the alimentary tract, especially such as

might cause weakness of the wall of the colon; laparotomies in general, except such as do not open the general peritoneal cavity, *e.g.*, suprapubic cystostomy; markedly incompetent sphincter or large, complete *fistula in ano*; orthopnea; emergency cases in general, because of the lack of preparation of the colon. Sutton (*Annals of Surg.*, April, 1910).

**LOCAL ANESTHESIA WITH ETHER.**—Local anesthesia may be obtained by means of a spray of ether, which, through its rapid evaporation, causes intense cold and deadens sensation locally. This is a useful procedure for minor surgical operations, especially for the opening of **abscesses.**

While the more rapidly acting ethyl chloride is now used far more frequently than ether, it is a fact that the induction of local anesthesia with the former often causes much pain through the rapid freezing of the tissues induced. The slower action of ether renders it superior to ethyl chloride in this single respect, *viz.*, absence of sharp preliminary pain.

**OTHER USES OF ETHER.**—As a **stimulant** in emergencies, *e.g.*, in **shock** and in **collapse** in **chronic heart disease** or in **acute infectious diseases**, ether is possessed of marked value. Hypodermic administration of 10 to 15 minims (0.6 to 1 c.c.)—or more in strong adults—is not infrequently followed by prompt reaction. One-half to 1 dram (2 to 4 c.c.) of Hoffman's anodyne may instead be given, either by mouth or hypodermically. The effect of ether on the heart and medulla is only of short duration, and should be supported with other stimulants. Its injection causes pain, and at least a part of the stimulating effect must be ascribed to

the sensory impulses conveyed to the centers from the irritated periphery.

Ether by inhalation found to be a good antidote of **cocaine** and **stovaine poisoning**. Engstadt (Jour. Amer. Med. Assoc., March 19, 1910).

Ether, whether as a vapor or liquid, has a bactericidal action. Vincent's typhoid vaccine is sterilized by ether instead of by heat. It never fails to sterilize albuminous culture media. It is therefore valuable in **septic wounds, abscesses and sinuses, peritoneal infections, pleuritic infections, and joint cavity infections**. J. Saliba (N. Y. Med. Jour., July 8, 1917).

The writer tested the bactericidal power of ether vapors on the streptococcus, staphylococcus, and colon bacillus. The germs were killed in about the same time as by 1 or 2 per cent. phenol—10 to 20 minutes. Philipp (Munch. med. Woch., July 28, 1922).

**As a Carminative** ether may with advantage be used internally in disorders attended with **flatulence** and distention, in order to stimulate the muscles of the alimentary tract and assist in the expulsion of gas. Relief from **colicky pains** may simultaneously or independently be secured. The drug may be given either in the form of Hoffmann's anodyne (*spiritus ætheris compositus*), in doses of  $\frac{1}{2}$  to 2 drams (2 to 8 c.c.), or, less pleasantly, in the simple spirits of ether, the dose of which is the same. Ether is also occasionally given as such, in doses of 15 or 60 minims (1 to 4 c.c.), either in ice-water or cracked ice, on a piece of sugar, or in capsules. It forms a clear solution with 10 parts of water.

**As an "Antispasmodic"** ether is sometimes useful in disorders in which some part or other of the nervous system is overexcited, *e.g.*, in **hiccough, asthma** and other spasmodic neuroses, in **chorea, in hysteria,**

and even in **migraine**. Thirty to 80 minims (2 to 5 c.c.) of ether in ice-cold water or in capsules, followed by a mouthful of water, are not infrequently promptly effective. Hoffmann's anodyne is often substituted for the pure ether.

W. W. Babcock administers the following combination by rectum when inducing mixed drug anesthesia (with morphine, scopolamine and apomorphine):—

*R Compound spirit of*

*ether* .....  $\bar{3}j$  (30 c.c.).

*Alcohol* .....  $\bar{5}ss$  (15 c.c.).

*Normal saline solu-*

*tion, to make* .....  $\bar{3}v$  (150 c.c.).—M.

To be slowly run into the bowel after the second injection of  $\frac{1}{16}$  grain (0.01 Gm.) of morphine and  $\frac{1}{100}$  grain (0.0006 Gm.) of scopolamine.

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## ETHYL AMINO BENZOATE

is the ethyl ester of paraminobenzoic acid. It is an odorless, tasteless, white, crystalline powder, very slightly soluble in water, but soluble in alcohol, ether, benzene, and fatty oils. It is decomposed by boiling or by the action of dilute alkalis. The drug, also known as *benzocaine* or *anesthesin*, became official in U. S. P. X (1926).

### PREPARATIONS AND DOSE.—

Ethyl aminobenzoate (*Æthylis aminobenzoas*, U. S. P.) may be used as a dusting powder, in ointment or in suppositories. Internally it may be given in the dose of 5 to 8 grains (0.3 to 0.5 Gm.).

### PHYSIOLOGICAL ACTION.—

This drug is a local anesthetic, similar in its action to orthoform, and used as a substitute for cocaine. It is said to be as efficient as orthoform, but free from an irritant or toxic action. Being practically insoluble, it cannot be given hypodermically, and its anesthetic action is purely local, but more prolonged than that of cocaine.

**THERAPEUTICS.**—Locally, ethyl amino-benzoate may be applied as an anesthetic in **nasal and laryngeal diseases**. It is also said to be of value in **urethritis**. It may also be used locally in **wounds, burns, ulcers, and painful skin diseases**. Internally it has been given for the relief of pain in various forms of **gastralgia**, and in **gastric ulcer and carcinoma**. H.

**ETHYL BROMIDE** (*athylis bromidum*).—Ethyl bromide, or hydrobromic ether, is an anesthetic prepared by combining bromine with alcohol in the presence of phosphorus. It was discovered by Sérullas, a French chemist, early in this century. It is an extremely volatile and colorless liquid, sweetish to the taste, and possessing an alliaceous odor. It is insoluble in water, but readily soluble in alcohol and ether. It presents the advantage over ether in not being inflammable. It is decomposed by sunlight and contact with the air.

Ethyl bromide is quickly eliminated from the system, and its after-effects are slight. Another preparation—ethylene bromide—is frequently dispensed instead of the bromide of ethyl; it causes nausea when inhaled, and in no way possesses the qualities of the latter. Ethyl bromide is, however, quite frequently found impure in the shops, and to this cause are due many of the untoward results met with.

**PREPARATIONS AND DOSE.**—Bromide of ethyl cannot be used for prolonged operations, owing to its high volatility. The dose, which varies with the age of the patient, should not exceed 6 drams (24 c.c.), 45 minims to 3 fluidrams (3-12 c.c.) being sufficient to induce anesthesia. For children, the dose should not exceed 16 minims (1 c.c.) per year of age. It should be administered rapidly with little or no air. The administration of bromide of ethyl should not be prolonged beyond two minutes.

The operation may usually be begun twenty seconds after the first inhalation.

**PHYSIOLOGICAL ACTION AND UNTOWARD EFFECTS.**—The dominant action of bromide of ethyl is said to be on the respiratory system, acting as a depressant, but only when given in excessive doses does it cause dangerous symptoms. It also lowers blood-pressure to a slight degree and slows the pulse, the latter being due to

its action on the inhibitory nervous mechanism of the heart.

This drug frequently leaves a garlic-like taste in the mouth and gives a similar odor to the breath, but it rarely produces other disagreeable symptoms.

It causes death by arresting the heart's action, and the cases should be watched as if chloroform were being administered,—respiration and pulse simultaneously. The preliminary preparations for its administration are the same, and the recumbent position obligatory under all circumstances. Arrest of the heart may be caused, however, through vasomotor influence originating in an intoxication by compounds formed in the system.

Two cases of ethyl bromide poisoning occurring in workmen engaged in the making of the drug. The noteworthy symptoms were sudden weakness and giddiness, along with disturbances of vision and dyspnea. With more severe poisoning or in more easily affected persons, psychic disturbance, possibly reaching to frenzy combined with delirium, occurred. It is remarkable that the most violent symptoms did not occur till the lapse of some days in the worst case. Experiments on rabbits with the drug showed diminution of spontaneity, gradual loss of power, then marked slowing, and, lastly, paralysis of respiration with epileptiform convulsions. The heart and vessels were affected very late. These experiments agreed with observations on men, in so far that the poisoning process did not cease with cessation of the inhalation, as is the case with other gas-forming poisons—*e.g.*, ether, chloroform, ethyl bromide—but continued to increase in intensity, and the animal died several hours after stoppage of the administration. Jaquet (*Deut. Archiv f. klin. Med.*, Bd. lxxi, 11fte. 4-5, 1901).

Rules for the use of ethyl bromide: Do not use ethylene bromide. Do not use an old or impure solution. Do not administer it in repeated and small quantities. Give *en masse*; admit no air. Do not continue its administration longer than one minute. Another essential to success in the use of ethyl bromide in these operations is that the operator shall be quick in his work, and,



in order that this may be true, a small and accurate instrument must be used. A. R. Solenberger (Jour. Amer. Med. Assoc., April 18, 1903).

Deaths from the use of the bromide of ethyl appear to have occurred chiefly some years ago before the sources of danger were understood. No death has been reported since 1897. The rapid anesthesia produced by bromide of ethyl, its short duration, the quick return to consciousness, and the absence of unpleasant effects are very striking.

The majority of the deaths reported have been due either to excessive dose or to impurity. It should be administered by means of a mask covered with impermeable cloth, so as to exclude the air. Unsuitable persons are young children and those suffering from anemia, Bright's disease, fatty degeneration, and alcoholism. Vomiting occasionally occurs.

One drawback of bromide of ethyl anesthesia is that the muscles do not usually become relaxed. In mouth operations a gag should be inserted before the operation is begun. (Huggard.)

**THERAPEUTICS.**—Ethyl bromide is best used in short operations, as opening **abscesses** and **boils**, and may also be used in **chorea**, **epilepsy**, and other spasmodic diseases.

Montgomery has used ethyl bromide for anesthetic purposes in **labor**, and minor **gynecological operations**. As the drug does not cause uterine relaxation, post-partum hemorrhage is less likely to occur after its use.

The writer has used ethyl bromide in **dentistry** in 15,032 extractions, and considers it the best anesthetic to employ for these cases. Owing to the spastic condition which usually develops, the patient should be firmly tied to the chair and a suitable mouth-gag should be inserted before anesthesia is begun. A preliminary examination of the heart is often necessary to quiet the patient. From 10 to 20 c.c. (160 to 320 minims) of the anesthetic are then poured on a folded napkin and placed over the patient's face, so that he can inhale sufficient air before the narcosis is complete. It is not necessary to pay much attention to the pulse or corneal reflex, as the first signs of too deep anesthesia

will be cessation of respiration and cyanosis.

It is important that a pure preparation be used and that this be kept well stoppered. It is often difficult to determine the proper moment for operating, but it is usually not necessary to wait for complete relaxation.

Among after-effects, vomiting is less common than after chloroform, and occasionally urine and stool are passed. The patients recover rapidly, and can generally go home without assistance.

The reason why ethyl bromide has not become more popular is probably because impure preparations are often employed. Breithach (Merck's Archives, Oct., 1910). S.

**ETHYL CARBAMATE.** See URETHANE.

**ETHYL CHLORIDE.**—Chloride of ethyl (monochlorethane) is a gas at ordinary temperatures, but which, when compressed, becomes a colorless, very inflammable liquid, boiling at 54.5° F. (12° C.). When ignited it burns with a green flame. It has an aromatic, sweet taste and an ethereal odor. It is exceedingly volatile, which latter property renders it unfit for anything but ephemeral anesthesia. This property causes it to evaporate so rapidly from the skin when applied locally in the form of spray that the cutaneous temperature is lowered sufficiently to become insensitive. Hence its employment as a local anesthetic.

**DOSE AND PHYSIOLOGICAL ACTION.**—For internal use it has been given in doses of 10 to 60 drops dissolved in an equal quantity of alcohol. Accordingly 5 c.c. (75 minims) should never be exceeded. When thus taken it has a stimulating action. When ethyl chloride is inhaled its chief effect appears upon the circulation and respiration, there

being a marked lowering of the pulse rate and the blood-pressure; the respirations are at first increased in depth and frequency. Its action resembles that of chloroform. Large doses cause cessation of cardiac and respiratory movements.

Sprayed on skin or mucous membrane, it causes them to become white, cold, and insensitive by the process explained above.

After an experience of 620 cases, the writer has satisfied himself that arterial tension, as a rule, is lowered during the administration of ethyl chloride, but that the pulse during deep narcosis becomes rather slower than normal and usually preserves its regularity. Respiration is markedly stimulated both in frequency and depth during deep anesthesia; the color is improved, due to vasomotor dilatation, which sometimes results in sweating and in one instance gave rise to a well-marked rash, like the ordinary ether rash. Adults as well as children take ethyl chloride very well and quietly, and very quickly pass under its influence. Any trouble during induction usually occurs with hysterical people, drinkers, smokers, and strong men. When excitement takes place, it is due to the too free admission of air, and yet at the same time a free use of air should be allowed. Failure of the anesthetic is also traceable to the too free mingling of air with the vapor. McCardie (*Lancet*, April 4, 1903).

In the open method of ethyl chloride administration the drug enters the system gradually and with free admixture of air; the shock given is more in the nature of a gentle push into unconsciousness as against the more violent and rapid rush into a state of insensibility in the closed method. With the open method there is no feeling of suffocation or desire to fight for air. It has been noticeable that there is very seldom any headache or feeling of great full-

ness in the head after the open method, both of which conditions are common after the closed. Ethyl chloride is very rapidly eliminated from the system, so that a few minutes after the completion of the operation the patient is quite fit to go home, a great advantage from the patient's standpoint as against ether or chloroform. Vomiting is rare unless the patient has swallowed some blood, in which case it will be brought up, but the nausea soon passes away. The writer does not recommend ethyl chloride for cases of more than five or ten minutes' duration. Hornabrook (*Austral. Med. Gaz.*, Nov. 20, 1911).

The writers find ethyl chloride anesthesia valuable even in operations of 45 minutes' duration. It is useful in military surgery because of the saving of time. There is seldom vomiting, and if any, it is very mild. It is valuable in shock, feeble pulse, etc. They have used it in 200 of 700 cases operated upon. Several cubic centimeters are given at first to obtain complete anesthesia; after that about 0.5 c.c. (8 minims) every 3 or 4 minutes. The 3 or 4 respirations of pure air when the mask is raised to give the ethyl chloride are generally sufficient to prevent asphyxia. Relaxation of the muscles is not so complete as with ether or chloroform. Carles and Charrier (*Progrès méd.*, xlii, 478, 1915).

**POISONING BY ETHYL CHLORIDE.**—Ethyl chloride inhaled in toxic doses produces poisonous effects similar to those of chloroform, but it is less of a cardiac depressant. Death results from paralysis of the respiratory centers and the heart. According to H. C. Wood, Jr., the statistics seem to indicate that, as regards mortality results, ethyl chloride stands between ether and chloroform, but this conclusion he regards as unfair. The anesthetics by ethyl chloride have

practically been all of but a few minutes' duration, and the prolonged anesthetics, which have to be credited with many of the fatalities of chloroform and ether, do not here come into consideration. The comparison should be rather with nitrous oxide gas. If we compare a commonly accepted mortality for nitrous oxide, 1 death in 1,000,000 anesthetics, with the figures for ethyl chloride, 1 in 6000, the danger of the latter is evident, as shown by many instances.

Ethyl chloride as a general anesthetic stands, as regards its mortality, next to chloroform, giving 1 death in 2075; ethyl chloride, 1 death in 2550. In the writer's fatal case, the patient, a large and muscular man, became suddenly very much cyanosed; respiration gradually ceased, though the pulse was still perceptible at the wrist, and in spite of restoratives death occurred. At the *post mortem*, eccentric hypertrophy of the heart, with fatty degeneration of the heart muscle, marked arterial sclerosis of the coronary arteries, and slight sclerosis of the aorta were found. Also, the heart and veins were filled with fluid blood, and there was edema of the lungs. Lotheissen (*Munch. med. Woch.*, May 1, 1900).

The writer collected from the literature 22 cases of death under anesthetization with ethyl chloride. Some of the cases were very bad subjects for any anesthetic. No less than 8 occurred during dental operations. Ethyl chloride is not a drug to be recommended off-hand, but requires, for its safe administration, discrimination, caution, and skill. In dental work it should not be given alone, but either in mixture with nitrous oxide in small doses for short cases, or in sequence with ether for longer cases. Luke (*Lancet*, May 5, 1906).

In 104 cases of ethyl chloride anesthesia, the duration of the anesthesia varied from one minute to fifty-five minutes, which time was that of a

hemorrhoid case. In those cases in which deep anesthesia was induced, nausea was as prevalent as would have been the case with chloroform. When it was given only to the primary stages, as for most operations, there was none or at most but little. Of these patients 15 were babies, several of the operations being circumcisions of from ten to twenty minutes' duration; 35 patients were children, 50 were adults, and 4 were quite aged. The only alarming results encountered were in 1 case, that of an old man with pronounced arteriosclerosis and subject to asthmatic attacks. He showed a marked cyanosis with unconsciousness for about one-half hour, which cleared up under a hypodermic injection of  $\frac{1}{75}$  gr. (0.0009 Gm.) of **atropine sulphate**. Manwaring (*Jour. Mich. State Med. Soc.*, Nov., 1906).

Case in which when surgical anesthesia was obtained there were clonic spasms of the legs and arms; respiration ceased, and the muscles of the jaws and neck were set in clonic spasm; cyanosis was marked; the eyes were fixed and staring, but the pupils remained contracted. Vigorous attempts to restore respiration were successful after there had been an actual suspension of respiration for about three minutes. Rugh (*N. Y. Med. Jour.*, vol. lxxxvi, p. 262, 1907).

Ethyl chloride was used alone in 947 cases, with ether in 4148, and with various other anesthetics in another series of cases. The youngest patient was 24 hours old, the oldest 84 years old. The fatalities were 5, all of them occurring when ethyl chloride was used alone. The fact that the ethyl chloride was given first and in all the cases in which the patients were considered bad anesthetic risks distorts the statistics. Three deaths occurred under ether during its administration alone in 1444 cases. The facts that ethyl chloride can produce deep anesthesia in from fifteen to twenty seconds, and that its danger signs are so easily overlooked, are

emphasized. In alcoholics and some others it produces muscular spasm and rigidity. W. E. Lee (Annals of Surg., Nov., 1908).

Case of collapse under ethyl chloride general anesthesia in a boy of 7 years. The collapse occurred during removal of adenoid vegetations, with enlarged tonsils, and came on in half a minute. There was considerable hemorrhage, but the child was revived by artificial respiration. Nielsen (Ugeskrift f. Læger, April 11, 1912).

The dangers of this anesthesia are of two kinds, to wit: (a) Excitation. This is due to too large initial doses of the drug. When it occurs the narcosis should be stopped and then recommenced, the anesthetic being administered progressively. (b) Deep narcosis is responsible for the great majority of fatal accidents. The writer prefers to continue the narcosis with ether, but generally begins with ethyl chloride. D. Kulenkampf (Deut. med. Woch., Oct. 18, 1917).

There are 2 types of symptoms of ethyl chloride over-dosage. The first or *spasm type* is seen in about 9 out of 10 instances, and is first indicated by a sardonic grin, the inspirations becoming crowing, and if the drug is continued, complete respiratory obstruction results. Cyanosis does not occur because the onset of spasm is so sudden. The systolic blood-pressure rises, as a rule. In treating these cases the mouth must be pried open, the tongue pulled out, and vigorous chest compression begun. The rapidity of elimination of the drug favors resuscitation. In the second or *depressed respiration type* the picture is that of collapse, with pupils widely dilated, ashen color, and feeble breathing. The pulse is slow, but of good quality and regular. Two or 3 forcible manual compressions of the chest bring about recovery, eliminating the excess of the drug. Guedel (Amer. Jour. of Surg., Jan., 1922).

**Treatment of Poisoning by Ethyl Chloride.**—When poisoning has been

induced by the inhalation of ethyl chloride, the tongue should be drawn forward, and caffeine, strychnine, or atropine given by hypodermic injection. Artificial respiration should be used faithfully, the head being lowered as in chloroform syncope. Amyl nitrite, ammonia, and warmth are also useful.

Case of a healthy young man in whom 40 drops were followed by sudden cyanosis and cardiac failure in spite of artificial respiration, oxygen insufflation, injections of pituglandol and adrenalin into the right ventricle, and direct cardiac massage. In this case the autopsy showed a persistent thymus. Hofmann (Munch. med. Woch., Feb. 3, 1922).

Sajous advises that vasodilators, such as amyl nitrite and nitroglycerin, be used in the early *spasm* period and the stimulants and vaso-constrictors, such as strychnine, caffeine, etc. in the *depression* or cardiac, vascular and respiratory failure period.

Ethyl chloride should be used only for minor or short operations such as removing tonsils, adenoids, opening abscesses thoroughly, removing toenails, scraping sinuses, and other small operations requiring one minute to a minute and a half.

Ethyl chloride is the best anesthetic known for single-dose cases—those in which anesthesia is induced, the mask removed, and the operation performed without further administration. While its effects are transient, it is a powerful anesthetic and should be carefully administered, and the patient properly prepared.

While for an adult of the ordinary type, nitrous oxide is the best, for certain operations on the eye, mouth, and nose which cannot be satisfactorily performed under non-continuous gas anesthesia, ethyl chloride either alone or combined with nitrous oxide gas has proved a valuable meas-

**ure.** For single-dose cases in adults, except in case of big, muscular men, the writer prefers the nitrous oxide and ethyl chloride mixture. Equally as good results can be obtained with smaller doses of ethyl chloride as when the drug is administered by itself. J. H. Chaldecott (*Clinical Jour.*, Aug. 1, 1906).

Ethyl chloride in operations on the throat in children is very satisfactory. It does not require to be given to deep anesthesia, and the child is soon able to arouse sufficiently to cough all material out of the throat and larynx. The author has performed over 1000 operations on the throat in children. E. M. Sill (*Med. Record*, Oct. 23, 1909).

In such operations as **circumcision, rib resection, removal of finger or toe nails, extraction of teeth, opening abscesses, and the removal of tonsils and adenoids**, ethyl chloride general anesthesia is of great value. The after-effects are generally mild; sometimes there is headache, and in about 1 out of 7 cases vomiting occurs. W. E. Lee has reported 5575 cases with 5 deaths, all of which were bad risks. Webster (*Amer. Jour. of Surg.*, Jan., 1922).

The most striking feature of ethyl chloride is the rapidity of its action. The patient is unconscious usually in forty-five seconds, and it is a mistake to keep the inhaler on longer than fifty to sixty seconds. It is possible to **amputate** a finger or toe during one administration of ethyl chloride. The stitches, however, may have to be deferred until the patient has recovered his senses (Lytton Maitland).

When administered carefully and for short periods only, it is apparently free from danger. It is not suitable for the reduction of fractures and dislocations on account of failure in producing thorough muscular relaxation. Its usefulness deserves wider recognition among members of the profession. Hagler and Bowen (*Surg. Gynec. and Obstet.*, Mar., 1918).

**Local Anesthesia.**—Ethyl chloride is usually dispensed in large tubes, one end of which is drawn out to a fine point, or in tubes closed by an automatic cap. When the former are used, the point is broken off, and the tube held in the hand, at a distance of from six to ten inches from the part to be anesthetized. The heat of the hand causes the liquefied gas to issue in spray-form. By its rapid vaporization the part soon becomes frozen and ready for operation. As the skin hardens under the ethyl chloride the exact limits of the operation must be determined beforehand. The highly inflammable nature of this agent must be remembered, and operations must be done at a good distance from gas and other flames or by electric light. The absence of unpleasant after-effects and of any influence on the sensory centers of the brain are its advantages over some other agents used for local anesthesia. It is used in the treatment of **ingrowing toe-nails, the opening of abscesses, removal of ganglia**, or for any painful skin incision. If the liquid is ignited as it issues from the broken tip, the flame thus produced may be used to cauterize septic or aseptic wounds or for cutaneous cauterization.

**Neuralgia.**—Ethyl chloride in spray has been used with success in **supra-orbital and facial neuralgia, sciatica, neuralgia of the breast**, upon the painful joints of incipient **gout, scrotal pruritus** (diabetic), and in **migraine**. From 2½ to 5 drams (10 to 20 c.c.) may be used as a spray at one sitting, the lesser quantity usually being sufficient.

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Philadelphia.

**ETHYLHYDROCUPREINE or OPTOCHIN**, introduced in 1913, is a valuable aid in pneumococcal infections of the eye, according to William Zentmayer (N. Y. Med. Jour., Feb. 24, 1917). It often acts as a specific in **pneumococcal ulcers of the cornea**, especially if the treatment is begun before active tissue destruction. The evidence as to its value in corneal and conjunctival diseases due to other organisms is as yet insufficient. J. S. Wyler (Lancet-Clinic, Dec. 25, 1915) found that, as mentioned by Grunert, it is of value in acute and mild **subacute infections of the lachrymal sac**. In 2 cases with long standing itching and redness of the eye, the writer obtained analogous results. In the first, much stringy mucus was being secreted, epinephrine and novocaine alone bringing but temporary relief. Instillation of 1 per cent. ethylhydrocupreine solution, every 2 hours, brought absolute and persistent comfort. In 3 cases of trachoma improvement took place under a 2 per cent. solution.

Pneumococci found in 5 per cent. of normal eyes at all ages, with 11 per cent. in the elderly. Vaccine and serotherapy having proved disappointing, our main reliance is on ethylhydrocupreine in superficial **ulcus serpens** and to ward off postoperative infection, painting the ulcer cautiously with a 2 per cent. solution about 3 times a day. With beginning infiltration, the strength is increased to 5 per cent., but this may entail iritis if kept up too long. Lunds-gaard (Hospitallstidende, June 11, 1925).

**Internal Use.**—One of the chief disadvantages of ethylhydrocupreine is its toxic side action. G. H. Oliver (Brit. Med. Jour., Apr. 22, 1916) had a patient who received a total of 120 grains (8 Gm.) of the drug in 5-grain (0.3 Gm.) doses at 3-hour intervals, with resulting blindness amounting to bare perception of light. Schiotz (Norsk Mag. f. Lægevid., June, 1917) also reported a case of transient blindness in a sailor of 48 after optochin given for pneumonia. Vision was considerably reduced, but not enough to incapacitate him. He became color-blind and the visual field much restricted and papilla grayish. There was also considerable hemeralopia.

**ETHYLENE.**—Ethylene is a gas having the chemical formula  $\text{CH}_2:\text{CH}_2$  and contained in illuminating gas to the extent of about 4 per cent. It is generally prepared from alcohol by dehydration. It has been found by Luckhardt and J. B. Carter (Jour. Amer. Med. Assoc., Mar. 17, 1923) to possess decided anesthetic properties, with a freedom from side effects which renders it in certain respects superior to nitrous oxide. Various animals were anesthetized with a 90 per cent. ethylene mixture with oxygen in  $\frac{1}{2}$  the time required for anesthesia with a like nitrous oxide mixture. A dog was anesthetized for 45 minutes 15 times in 3 weeks without untoward symptoms. Observations in man showed that deep surgical anesthesia can be rapidly induced without any sense of asphyxia; in fact, with a sense of well-being and comfort. Analgesia comes on long before surgical anesthesia. No cyanosis was ever observed. Some excitement, especially laughter, at times preceded or followed anesthesia. Recovery was always rapid, with but slight and transient after-effects. Anesthesia may be maintained in the absence of dyspnea, asphyxia, or effects on blood-pressure, and with complete muscular relaxation. It may be used in obstetrics, complete analgesia being possible with 80 per cent. of ethylene. Its use seems feasible where nitrous oxide is contraindicated, as in children, diabetics, old age, advanced arteriosclerosis, high cerebral pressure, brain operations, and major operations in general.

According to J. S. Lundy (Jour. Amer. Med. Assoc., Aug. 2, 1924) poor risk patients relax satisfactorily, as a rule, with a mixture of 75 per cent. ethylene and 25 per cent. oxygen, and in them the optimal result is obtained. Aurelius (Minn. Med., Aug., 1924) reported on 300 cases, of which 194 were major surgical procedures. The age limits ranged from 2 months to 77 years, and for both extremes ethylene seemed an ideal anesthetic by reason of the ease and rapidity of induction, the quiet, undisturbed respiration, regular pulse, and absence of postoperative shock, lung involvement or severe vomiting. The average duration of anesthesia was 43 minutes, with 7 cases consuming over 2 hours. In 40 cases ether was used at some time, either to aid relaxation or during induction in excitable

subjects. In most cases relaxation was very satisfactory, being definitely more complete than with nitrous oxide. General convalescence was rapid and uneventful, and gas pains caused little complaint. The gas is less costly than nitrous oxide. It entails very little risk in pulmonary conditions.

The *disadvantages* of ethylene are enumerated by Moots (U. S. Naval Med. Bull., Apr., 1924) as follows: 1. It is inflammable and should not be used with a cautery or electric spark in the same room. 2. The odor is garlic-like and unpleasant, but not pungent or irrespirable as ether is in such concentrations. 3. Respiro-cardiovascular depression is greater than in gas-oxygen, but less than with ether. The writer, however, fully recognizes the advantages of ethylene: 1. Relaxation; 2, rapid action; 3, infrequency of nausea, and 4, easy administration. S.

## EUCAINE HYDROCHLORIDE

(*beta-eucaine hydrochloride*) is a synthetic substance approximating cocaine as to its chemical formula. It is termed *beta-* or *B-* eucaine to distinguish it from *alpha-eucaine*, an earlier but less valuable substance proposed by the originator of both, Vinci. The free base of *beta-eucaine* is nearly insoluble in water, but the hydrochloride, which is official as *Eucaïne hydrochloridum*, U. S. P., is soluble.

### PREPARATIONS AND DOSE.—

*Eucaïne hydrochloride* is employed in lieu of cocaine to produce local anesthesia. The strength of the solution to be used depends upon the locality to which it is applied. A 2 per cent. solution is strong enough to produce anesthesia of the eye, while a 5 to 10 per cent. solution is required for mucous membranes. Stronger solutions can be used, however, without fear of producing toxic phenomena. It forms a permanent 3½ per cent. solution in water, and can be boiled without change.

Eucaïne hydrochloride is also used in *infiltration anesthesia*. The procedure is as follows: Powders are kept in stock in the operating room containing 0.02 Gm. (3 grains) of *beta-eucaine* and 0.8 Gm. (12 grains) of pure sodium chloride. At the time of the operation one such powder is dissolved in 100 c.c. (3½ ounces) of boiling distilled water, and when it is cooled sufficiently 1 c.c. (15 minims) of adrenalin

chloride solution (1:1000) is added; 100 c.c. (3½ ounces) of the resulting liquid contain 3 grains (0.2 Gm.) of *B-eucaine* and 0.015 grains (0.0009 Gm.) of adrenalin chloride. The whole 100 c.c. (3½ ounces) may be used at one infiltration anesthesia, but according to Barker from 50 to 60 c.c. (1½ to 2 ounces) usually suffices, even in operations as for hernia and castration.

*Eucaïne lactate* is much more soluble than the hydrochloride and is employed when strong solutions (5 to 20 per cent.) are required. When local ischemia is desired epinephrin (1:1000) is added.

**PHYSIOLOGICAL ACTION.**—The manner in which eucaine hydrochloride produces anesthesia is not clearly established. It does not cause constriction of the arterioles as does cocaine, but paralyzes the sensory terminals without causing irritation or injury to the tissues.

Internally, eucaine hydrochloride was found by Ver Eecke to act as follows:

In the frog it determines successively excitation, convulsions, and paralysis. The return to the norm is accompanied by convulsions, and later by hyperexcitability. The fatal dose is 0.16 Gm. (2½ grains) per kilogram (2½ pounds). In the warm-blooded animals it produces excitation, which is followed by convulsions and, finally, death from asphyxia. There is no paralyzant dose. The fatal dose in the guinea-pig is from 0.049 to 0.052 Gm. (¾ to ¾ grain) per kilogram (2½ pounds). There is no cumulative action of the poison; on the contrary, the organism may accustom itself to increasing doses of the drug. Cocaine has twice the toxic action which is possessed by eucaine. Eucaïne hydrochloride acts on the heart principally by paralyzing the intracardiac motor center and secondarily it alters the muscular fiber of the heart. It lowers the blood-pressure by diminishing the peripheral resistance. It directly stimulates the respiratory center in the medulla. The paralysis of this center which occurs in fatal poisoning is not the result of the direct action of the poison, but is due to asphyxia, which in its turn is caused by an excess of carbon dioxide in the blood. It increases diuresis, accelerates nitrogenous, phosphorous, and chlorous metabolism, and produces glycosuria, but only

during the presence of intense convulsions. It does not appear to be eliminated by the kidneys; on the other hand, it probably undergoes a chemical decomposition in the body. Instilled in the conjunctival sac eucaine hydrochloride first produces anesthesia of the conjunctiva and, finally, of the cornea at the same time that it rapidly lowers the intraocular pressure. It reduces the vitality of the red blood-corpuscles and produces fatty degeneration of the heart and of the involuntary muscles.

**POISONING BY EUCAINE.**—Intoxication by this agent is extremely rare, a great advantage over cocaine (*q.v.*). Kraus (Deut. med. Woch., B. xxxii, No. 2, 1906) witnessed a case in a robust, phlegmatic man of 40 years, on whom internal urethrotomy had been performed the day before, under local anesthesia with 10 c.c. (2½ drams) of a 2 per cent. solution of eucaine hydrochloride.

The injection was repeated the next day when he came to have the cut stricture stretched. Almost at once he felt faint and became partly unconscious, with increasing dyspnea, distress and chills, while the breathing grew shallower and shallower. The conditions lasted in all for an hour or an hour and a half. The patient was able to eat then, but did not sleep much that night and found that he was somewhat forgetful for a day or so afterward. There was no actual collapse. Treatment was with **wine** and **camphor**, **faradization** of the phrenic nerves in the **neck** and inhalation of **oxygen**. It was the first time that any mishap has been observed from the use of beta-eucaine in Lewin's Urologic Polyclinic, although it is in daily use there.

Two cases of intoxication from eucaine hydrochloride have also been reported by Marcinowski. In 1 case the patient had a transient syncope, but she was subject to fainting. In the other case, after injection of 1.5 c.c. (23 minims) of a 10 per cent. solution the patient exhibited tonic and clonic spasms, which gradually subsided after fifteen minutes, but were followed by stupor and weakness, the symptoms all passing away by the end of six hours. Dolbeau reported a similar case after intravenous injection of eucaine hydrochloride, and Simon has mentioned transient

headache and vomiting in a man whose bladder had been filled with 80 c.c. (2½ ounces) of a 4 per cent. solution for a Bottini operation.

**Treatment of Eucaine Poisoning.**—The inability of eucaine to produce contraction of the peripheral blood-vessels, and the physiological effects of its internal use tend to suggest that the phenomena of intoxication are due, in oversensitive individuals, to paresis of the vasomotor terminals as well as that of the sensory terminals. Stimulation is therefore indicated. Besides **oil of camphor** injections, inhalations of **oxygen** and **faradization** of the phrenics were employed successfully by Kraus. **Epinephrin solution** (1:1000), 20 drops in saline solution intravenously, suggests itself as the most efficient measure, owing to the specific stimulative action upon the arterioles.

**THERAPEUTICS.**—For *local use*, eucaine lactate is preferable owing to its greater solubility and the fact that stronger solutions are required than for infiltration anesthesia. Harris (Amer. Med., Dec., 1905), with a 10 to 15 per cent. solution, was able to perform septal and other serious nasal operations. To sustain the effect he added epinephrin, as shown in the following formula:—

**R** *Eucaine lactate.* 0.52 Gm. (8 grains).  
*Sodium chloride.* 1.40 Gm. (21 grains).  
*Distilled water.* 52.00 c.c. (14 drams).  
*Adrenalin chloride sol.*..... 1.00 c.c. (16 minims).

This was applied on cotton for ten minutes. When a septal or a serious operation was to be performed he injected 20 to 30 minims (1.3 to 2 c.c.) of the solution at two or three points in the septal mucosa, thus avoiding all pain.

The writer uses a 12 per cent. solution of lactate of beta-eucaine to anesthetize the mucous membrane in nose, throat, and ear troubles. It does not disturb the circulation or shrink the tissues, hence in operations on the turbinals the amount of tissue which should be removed is easily estimated. For **turbinotomy** he uses a 12 per cent. solution on a cotton tampon, which is allowed to remain five minutes, and is then replaced by a fresh one, which



remains a similar time. A 5 per cent. solution dropped into the conjunctival sac causes more smarting than a 4 per cent. solution of cocaine, but there is neither hyperemia nor anemia, and vision is in no way disturbed. The anesthetic effect is equal to that of a 4 or 5 per cent. cocaine solution. H. B. Ellis (Calif. Med. and Surg. Reporter, March, 1905).

Judging from his experience with beta-eucaine which extends over ten years, the writer prefers this anesthetic because it can be sterilized, does not irritate, and invariably produced a most complete anesthesia and causes less toxic manifestations than like agents, when used in an equal strength or quantity. In fact, when beta-eucaine is employed in  $\frac{1}{8}$  per cent. solution in **anorectal operations**, the patient rarely complains of pain or dizziness or turns pale, becomes excited or faints during or following the operation. This is partly due to the non-toxic effect of the drug, and partly to the fact that the solution is very weak and escapes during or following operation. S. G. Gant (Merck's Archives, Nov., 1910).

For **infiltration anesthesia** eucaine was found by Barker and many others to possess analgesic properties little, if at all, inferior to cocaine. One hundred c.c. ( $3\frac{1}{2}$  ounces) of a fluid containing 0.2 per cent. beta-eucaine, with epinephrin, can be used in an ordinary case if necessary, and is quite sufficient for most operations. Twice as much may be injected without ill results. The duration of the insensibility is secured by the admixture of epinephrin. Without it sensation is only abolished by eucaine for about fifteen minutes; with it, for three or four hours. But the analgesia is produced more slowly when epinephrin is employed. It is therefore well, before all larger operations, to wait some thirty minutes after injection to allow time for the insensibility to become fully developed. After this the effect appears to deepen for a couple of hours. Waiting has another advantage, in that by the time operation is begun the artificial edema has disappeared and details are very clearly

seen. Rapid injection is to be avoided; sudden distention of the tissues is disagreeable, if not painful. The fluid should not be used cold nor too hot, for the same reason. All dragging on the parts is to be avoided, lest structures be pulled upon which lie beyond the area of infiltration.

Various authors have failed to see depressing effects follow the use of beta-eucaine in a long series of operations, including **abdominal sections, hernia operations, amputations, orchidectomy**, removal of **cyst of thyroid**, removal of silver wire from around the patella, operations for **fistula in ano, varicose veins, hydrocele, varicocele**, etc.

The area of infiltration of the skin should be made directly in the line of the proposed incision and should be long enough to allow of easy exposure of the tissue beneath. When the operation is to extend into the deep tissues it is best to infiltrate step by step and not to attempt to infiltrate the whole tissue at once. Among the operations performed under his anesthesia were **partial thyroidectomies for exophthalmic goiter; ligation of arteries; radical operations for malignant disease of the breast; gastrostomies; gallstone operations; appendectomies; renal decapsulation; nephrectomy; nephrotomy; hysteropexies; myomectomies; radical inguinal and umbilical herniotomies; perineal cystotomies, operations for hallux valgus**. Wither- spoon (St. Louis Med. Rev., Mar. 24, 1906).

Eucaine has also been used to obtain spinal anesthesia, but its indications for this purpose will be considered under the heading of SPINAL ANESTHESIA. W.

**EUCALYPTUS.** — Eucalyptus U. S. P. is the leaves from the older parts of the *Eucalyptus globulus labillardierei*. The eucalyptus, or blue-gum tree, is a tall, evergreen tree, a native of Australia, but now grown all over the world. From the leaves the oil of eucalyptus is obtained by distillation, and from this oil, by re-distillation with caustic potash or

calcium chloride, a camphoraceous body is obtained which is known as *eucalyptol*. The latter is the refined product.

It was once thought that, as the tree grew easily in marshy districts and drained the soil of water, it would diminish the malaria miasm of low, swampy regions, and in that way prove a prophylactic against malaria. Laveran has shown, however, that the organism causing malaria troubles is, in all probability, taken into the body through the media of food and drink, and that the planting of the eucalyptus trees does not diminish the paludal fevers. The prevailing view that mosquitoes are the main intermediaries through which the infection occurs also tends to diminish faith in eucalyptus as a prophylactic, though the tree itself tends to keep these pathogenic insects away.

The leaves have a camphoraceous odor and a pungent, bitter taste, and yield a volatile essential oil, the oil of eucalyptus, which is the active principle. Eucalyptus oil is a faint-yellow, sometimes colorless liquid, having a characteristic aromatic odor and a pungent, cooling taste, and being soluble in alcohol and in bisulphide of carbon. The value of the oil depends upon the amount of eucalyptol present.

Eucalyptol is a colorless liquid, with a strong, aromatic, camphoraceous odor; is slightly soluble in water, but easily soluble in alcohol, ether, and fatty oils.

By treating oil of eucalyptus with hydrochloric acid Anthoire has obtained a white, micaceous, scaly substance, hygroscopic in nature, called eucalypteol. It is soluble in alcohol,

ether, chloroform, and oils, but almost insoluble in water and in glycerin. It is not poisonous, and is tolerated by the stomach.

#### PREPARATIONS AND DOSE.

—*Eucalyptus*,  $\frac{1}{2}$  to 2 drams (2 to 4 Gm.).

*Fluidextractum eucalypti* (fluid-extract of eucalyptus), 10 minims to 2 drams (0.6 to 8 cc.).

*Oleum eucalypti* (oil of eucalyptus), 5 to 20 minims (0.3 to 1.25 c.c.).

*Eucalyptol*, 1 to 15 minims (0.06 to 1 c.c.).

*Eucalyptol*, 24 grains (1.5 Gm.) daily, in divided doses.

#### PHYSIOLOGICAL ACTION.—

Applied externally, the oil is a decided irritant, and causes heat and redness of the part, due to dilatation. When inhaled it causes an increase of the saliva and of the bronchial secretion. When taken internally in medicinal doses it produces a feeling of warmth and stimulation, with increased secretions, while larger doses are productive of disordered digestion, diarrhea with loose stools having the characteristic odor of the oil, and symptoms of renal and cerebral congestion. When larger doses are used there are noticed a rapid, weak pulse, general excitation, and restlessness; decrease of body heat, lower arterial pressure, irregular and weak respirations; muscular weakness, especially of the lower limbs; and death from respiratory paralysis. The drug is eliminated by the bronchial mucous membranes, the skin, the kidneys, and the bowels. The urine may have the odor of violets, as noticed after the ingestion of the oil of turpentine. The oil of eucalyptus, like most aromatic oils, is an antiseptic and a germicide, and in sufficient strength

it inhibits the growth of micro-organisms in culture media. Eucalyptus is a powerful diuretic. An increased excretion of urine is said to follow its internal use.

#### POISONING BY EUCALYPTUS.

—Toxic doses of eucalyptus give rise to the symptoms of gastrointestinal irritation, renal and cerebral congestion, impaired circulation, muscular weakness and paralysis, and finally death by respiratory failure. Cases of poisoning are not frequent.

Case of poisoning in which between 2 and 3 teaspoonfuls of oil of eucalyptus had been swallowed. The severe stupor, myosis, and hypothermia which followed suggested opium poisoning. Stertorous breathing, however, was absent. Recovery. F. C. Wood (Brit. Med. Jour., Jan. 27, 1900).

Case of eucalyptus oil poisoning. A boy, 6 years of age, who had occasionally been in the habit of getting a drop or two of eucalyptus oil on sugar was given by mistake 1 dram. Pain and severe vomiting appeared. The vomiting continued without cessation of any length with diarrhea. The boy became drowsy, then semi-comatose. After two or three hours of external stimulation, the comatose condition appeared to pass off, and the child was allowed to sleep. He slept well and next morning, beyond being a little tired, was quite himself again. The breath had a smell of eucalyptus oil for three days. There was never any irritation of the urinary tract. The poison showed itself by gastrointestinal irritation and cerebral paresis. Foggie (Brit. Med. Jour., Feb. 18, 1911).

Eucalyptol poisoning has followed both overdoses and small doses of the drug; some persons have an idiosyncrasy for it. Two different syndromes were noted in the after effects: First, nervous system involvement with collapse; second, dermatitis. In the nervous type the patient became seriously

ill shortly after the dose. Vomiting, diarrhea, and coma might follow. Vomiting should be induced to prevent further absorption of the poison. Skin lesions were often associated with the nervous lesions. Several fatalities have been reported from time to time. A greatly increased use of eucalyptol has resulted from its employment as a solvent for the Dakin solution, dichloramine-T. L. F. Barker and L. G. Rowntree (Bull. Johns Hopkins Hosp., Oct., 1918).

**Treatment of Poisoning by Eucalyptus.**—In mild cases the gastrointestinal symptoms should be ameliorated through the use of **morphine**, **bismuth**, **lime water**, etc. In severe cases, when the circulation and respiration are profoundly affected, the use of **caffeine**, **strychnine**, and **atropine** by hypodermic injection is advised.

**THERAPEUTICS.** — Eucalyptus has a selective action upon the mucous membranes, being excreted through them. To them it is a stimulant, antiseptic, germicide, and antispasmodic, and we find that its most beneficial action is exerted, therefore, directly upon the gastrointestinal tract, the bronchial tubes, and the genitourinary tract; indirectly upon certain mucous disorders more or less dependent upon the integrity of tissues and function of those organs. In general, it is contraindicated in acute inflammatory conditions. The tincture has been found very useful in the treatment of **hemorrhages** of various kinds.

The writer highly recommends the application of the tincture of eucalyptus for the arrest of any form of **hemorrhage**. He mentions 3 cases in which all means to stop the persistent hemorrhage failed, but the bleeding ceased immediately upon the application of the tincture of eucalyptus. One

case was that of a boy, who had a tooth extracted three days before, and had persistent hemorrhage from the socket. Another case was that in which there was profuse hemorrhage from the cut in the patient's foot, and in the last case the hemorrhage followed the application of a leech to the gum. He also calls attention to the use of this preparation as a dressing on lint after **circumcision** or other minor operations. A. Todd-White (Brit. Med. Jour., July 11, 1908).

**Gastrointestinal Disorders.**—In **atonic dyspepsia** and **chronic gastric or intestinal catarrh**, eucalyptus is one of the most useful stomachics. In **convalescence** from acute disease and in **debility from defective assimilation** it is a useful stimulant and tonic. In the **flatulence**, **cardiac palpitation**, and **hot flashes** of the **menopause** it is often of permanent benefit. It has been found useful in **cholera**, 5 minims (0.3 c.c.) being given in milk every quarter-hour for one hour, then every hour. On account of its antiseptic action, eucalyptus oil and eucalyptol have been used in **typhoid fever**, being administered in capsules.

**Bronchial Disorders.**—In **subacute** and **chronic bronchitis** eucalyptus loosens the secretions, stimulates and gives tone to the mucous membrane, and exerts, withal, an antiseptic action, especially in cases accompanied by free mucopurulent secretion. It is also useful in **bronchorrhea**. Oil of eucalyptus, in ointment suitable for inunctions, has recently been tried in **pulmonary tuberculosis**. The method seems worthy of trial.

The method of use is to direct that 1 teaspoonful of the preparation be thoroughly rubbed into the skin until it disappears, varying the locality with each application. The following formula was employed:—

R Olive oil ..... ℥ij (60 c.c.).  
Benzoinated lard.. ℥vj (180 c.c.).  
Cacao butter ..... ℥iv (120 Gm.).  
Eucalyptus oil .... ℥iiss (105 c.c.).

This amount contains 15 minims (1 c.c.) of eucalyptus oil, the major part of which reaches the circulation. In many instances the constitutional effects have been noted after one application. The most striking early effect was a change in the character and quality of the expectoration: having been yellow, viscid, and moderate in volume, it froths up and becomes white, free, easy to expectorate, and temporarily more abundant. Then follows a reduction in the amount of sputum, accompanied as a general rule by a continued improvement in the cough.

Coincidentally with these changes, the temperature ran a lower and more favorable course, the change usually beginning within twenty-four hours of the first administration. The patient generally reports a feeling of well-being which is known to be one of the characteristic effects of the drug. L. G. Pedigo (Therap. Gaz., March 15, 1913).

**Genitourinary Disorders.**—In **chronic cystitis**, **pyelonephritis**, and **chronic desquamative nephritis** eucalyptus has been recommended as an efficient remedy. In **subacute gonorrhea** Hare advises 6 minims (0.36 c.c.) each of eucalyptus oil and sweet-almond oil in a capsule after meals.

**Malaria Fevers.**—Eucalyptus has been praised as a remedy for **intermittent fever**, in the absence of quinine or where idiosyncrasy interdicts its use. It cannot take the place of quinine to arrest the paroxysms, or to prevent relapses at the septenary periods, but is more useful than quinine to reconstruct the damages in the organs of assimilation caused by malarial infection.

**Nervous Disorders.**—**Spasmodic asthma** is much relieved by eucalyptol given by steam inhalation. Cigarettes made from eucalyptus leaves alone, combined with stramonium, belladonna, tobacco, etc., give similar relief. **Pertussis** has been relieved by a mixture of 1 part each of eucalyptus oil and terebene, and 6 parts of alcohol, used in spray half an hour before meals and at bedtime (Hardwicke). **Malarial or congestive headache** may be relieved by oil of eucalyptus, 5 minims (0.3 c.c.) being given four or six times daily.

C. SUMNER WITHERSTONE.

Philadelphia.

**EUDOXIN** is a compound of iodine, bismuth, and phenolphthalein. It is a tasteless, odorless powder, having a reddish-brown color. It is insoluble and contains about 60 per cent. of iodine. The drug is not official.

**PREPARATIONS AND DOSE.**—Eudoxin may be given in the doses of 5 to 20 grains (0.3 to 1.3 Gm.) to adults. It may also be used as a dusting powder.

**PHYSIOLOGICAL ACTION.**—Locally, eudoxin acts as an astringent and a protective. Internally, the drug acts as an intestinal antiseptic and antifermentative.

**THERAPEUTICS.**—Locally, eudoxin is used in **burns** and **ulcers**, and has also been found of some value in certain skin diseases. It has also been used in some eye diseases. Castor oil, containing enough eudoxin to make a thick paste, may be found of value as a local application for **cracked nipples**.

Internally, eudoxin is of value in catarrhal inflammations of the bowels. It is also recommended in the **diarrheas** of children.

H.

**EUMYDRIN** is the nitrate of methylated atropine. It is a white, crystalline, odorless salt, slightly soluble in ether or chloroform, but readily soluble in water or alcohol. It is incompatible with alkaline solutions. The drug is not official.

**PREPARATIONS AND DOSE.**—Externally, eumydrin may be used in a 1 to 2 per cent. solution to produce mydriasis. It

may be given internally in the dose of  $\frac{1}{80}$  to  $\frac{1}{24}$  grain (0.001 to 0.0025 Gm.).

**PHYSIOLOGICAL ACTION.**—Eumydrin is a mydriatic and antihydrotic. It has been used in place of atropine, as it is said to act more rapidly and to be less toxic. Its effects wear off more quickly than when atropine is used. It is claimed that eumydrin has the peripheral action of atropine without its effect on the central nervous system.

**THERAPEUTICS.**—Eumydrin may be used locally in the eye to produce **mydriasis**. Internally, it is said to be of especial value in the treatment of **pertussis**, **night-sweats**, and **enuresis**.

Eumydrin is useful in functional and secretory neuroses of the alimentary tract, such as **hyperchlorhydria**, **gastralgia**, **intestinal spasm**, **perityphlitis**, etc., and in all conditions of the stomach and intestines in which belladonna or atropine is indicated. Eumydrin is much less toxic than atropine. Its dose is  $\frac{1}{80}$  to  $\frac{1}{15}$  grain (0.001 to 0.004 Gm.) three or four times a day, and it may be prescribed in pill, powder, solution or suppository. G. Haas (Therap. der Gegenwart, Nn. 3, S. 105, 1905).

Upon healthy and diseased irides, it acts, in equal doses with atropine, more slowly, with less energy, and its effect is not so lasting; on the other hand, it is less toxic and appears to have no influence upon the tension. It can be substituted for atropine in children, the aged, and when the latter is not well borne. In 0.5 per cent. solution it acts more rapidly than homatropine, but its effects last about ten hours longer; this can be decidedly shortened by pilocarpine, rendering eumydrin preferable when, for examination, dilatation of the pupil is desired. Del Monte (Arch. d. ophthal., July, 1906).

H.

**EUONYMUS**, or Wahoo, is the dried bark of the root of *Euonymus atropurpureus*, a plant of the United States. It occurs as curved or quilled pieces having a pale brownish-gray or ashy outer surface, and a whitish or light-brown, smooth inner surface. There are small, dark, scaly patches over the external surface. It has a distinct odor and a slightly bitter and

somewhat acrid taste. It is slightly soluble in alcohol or ether, and freely soluble in water. Euonymus contains a bitter, amorphous substance known as *euonymin*, atropurpurin, and several acids.

**PREPARATIONS AND DOSE.**—The average dose of euonymus is  $7\frac{1}{2}$  grains (0.5 Gm.).

*Extractum euonymi*, N. F. (extract of euonymus), is made by the evaporation of the fluidextract and the addition of powdered glycyrrhiza. Dose, 2 grains (0.125 Gm.).

*Fluidextractum euonymi*, N. F. (fluid-extract of euonymus), is made by the maceration and percolation of the drug with alcohol and water, followed by evaporation. Dose, 8 minims (0.5 c.c.).

**PHYSIOLOGICAL ACTION.**—Small doses of euonymus act as a tonic, increasing the appetite and the gastric secretions. It is a direct cholagogue, and a slow and mild laxative.

The drug has also been credited with some expectorant and diuretic action, and first increases and then decreases the excretion of uric acid. Large doses act as an intestinal irritant.

**THERAPEUTICS.**—Euonymus is useful in all hepatic derangements and is also used in indigestion and chronic constipation. It is also claimed to be of value in malaria and dropsy. H.

**EUPHTHALMINE HYDROCHLORIDE** is a colorless crystalline powder derived from beta-eucaine and is soluble in water.

**PREPARATIONS AND DOSE.**—Euphthalmine hydrochloride is used in a 5 to 10 per cent. solution, 2 or 3 drops of which may be instilled into the eye.

**PHYSIOLOGICAL ACTION.**—Euphthalmine is a prompt mydriatic. It has no anesthetic action, and does not produce any pain, irritation of the cornea, or increase in intraocular tension. The effect of euphthalmine disappears more rapidly than that of atropine. Its effect on the general system resembles atropine.

**THERAPEUTICS.**—Euphthalmine is used as a mydriatic in ophthalmoscopic examinations in place of atropine. The fact that its effects are relatively ephemeral, constitute an advantage when but a

single examination under a mydriatic is necessary.

The value of euphthalmine as a brief mydriatic is now well established, all observers being fully agreed regarding it. There is also complete agreement as to its freedom from danger of any injurious effect upon the cornea, such as strong solutions of cocaine are likely to produce. Regarding the risk of producing an outbreak of glaucoma with euphthalmine, while it is probably less than with any other mydriatic but cocaine, and most writers speak of it as *nil*, we must remember that every other new mydriatic has been put forward with the same assertion, but experience has in each case failed to substantiate the claim. Jackson and Schneideman (Amer. Jour. Med. Sci., June, 1900).

In many cases of cataract, central opacity of the lens precedes cortical involvement. If the pupillary aperture be narrow, as is generally the case in the aged, vision is greatly interfered with by such central opacity, which blocks the entire pupil, and where the condition is bilateral, the patient is unable to read or write. The operation of preliminary iridectomy usually performed under these circumstances may be impossible for two reasons: 1. General disease contraindicating operation. 2. Refusal of the patient to be operated. For several years the author has successfully used in these cases euphthalmine hydrochlorate, which, by its mydriatic effect, permits of vision through the uninvolved cortical portions of the lens. A mydriatic used for such a purpose must be shown to be entirely harmless, since it may have to be used for several years. In the use of euphthalmine the author has observed no untoward effects. Intraocular tension is not affected, accommodation is but rarely and very slightly influenced, and there are no secondary intoxicating effects. Sometimes there is a slight burning sensation of the conjunctiva in the first half minute after use. Mydriasis begins in twenty

minutes and lasts four hours with the 3 per cent. and seven hours with the 5 per cent. solution. To avoid the dazzling effect from the increased admission of light, the patient's ordinary glasses may be colored blue or greenish yellow. The drug must not be used after 6 P.M.; 1 or 2 drops after breakfast enable the patient to read in the morning, and 1 or 2 at noon, in the succeeding afternoon hours. With this procedure persons previously debarred from all work may, in part at least, resume their former occupation. A. Dufour (*Revue méd. de la Suisse Romande*, Jan. 20, 1910).

11.

## EUQUININE. See CINCINA.

**EUROPHEN.**—Europhen, or iododisobutylorthocresol, is the result of the action of iodine on isobutyl alcohol and orthocresol with zinc chloride by heat. It is allied to aristol and appears as a light, dull-yellow, amorphous, aromatic powder, which is soluble in alcohol, ether, chloroform, and oils, but insoluble in glycerin or water. It has an aromatic odor, like saffron, but has no taste. It is stable when kept dry. On prolonged exposure to moisture it is decomposed, setting free nascent iodine. If heated to 158° F. (70° C.) in the presence of water it is decomposed; hence heat should not be employed in making solutions of it. It contains 28.1° of iodine. It was introduced as a substitute for iodoform. Europhen is incompatible with the metallic oxides, all preparations of mercury, and starch.

### DOSE AND PHYSIOLOGICAL

**ACTION.**—Internally the dose is 1 to 3 grains (0.065 to 0.2 Gm.). By hypodermic injection (in a 3 per cent. to 10 per cent. solution in olive oil) the dose is 1 to 1½ grains (0.065 to 0.1 Gm.) once daily. Externally, it is used in 5 per cent. to 10 per cent. ointment, dissolved in olive oil or lanolin (5 per cent. to 30 per cent.), as a dusting powder (1 part to 3 of boric acid), in 10 per cent. gauze, or pure.

The therapeutic value of europhen depends upon the liberation of iodine when it is exposed to moisture. In this its action is similar to that of iodoform; but europhen parts with its iodine more

slowly, even under the most favorable conditions; and while it is thus less poisonous than iodoform it is also, for the same reason, less efficient.

On the other hand, it is more bulky, will go farther, and is less likely to cake than iodoform. Its properties are those of an antiseptic, antisyphilitic, and alterative. It exerts a polyseptic action upon bacterial growth.

**THERAPEUTICS.**—Europhen is not generally given by the mouth, although it has been administered in **syphilis**, in doses of ½ to 2 grains (0.032 to 0.13 Gm.). It is not considered poisonous; as much as 23 grains (1.5 Gm.) has been taken daily for three weeks without any appreciable disturbance. It is believed that europhen taken internally passes through the bowels almost unchanged. The hypodermic use of europhen has not met with much favor, and, although tried in the treatment of syphilis, it has not yielded the results anticipated. As a surgical dressing and in some **cutaneous disorders**, principally those presenting moist or secreting surfaces, europhen has found great favor.

Europhen has been highly recommended by Flick in the treatment of **pulmonary tuberculosis**. He introduces it into the body by means of injections, using the following formula:—

℞ *Europhen* ..... ʒij (8 Gm.).  
*Oil of roses* ..... ℥ij (1.2 c.c.).  
*Oil of anise*,  
*Oil of gaultheria*,  
 of each ..... fʒij (8 c.c.).  
*Olive oil*, enough to  
 make ..... fʒv (150 c.c.).

The quantity to be used is proportionate with the age of the patient.

**Wounds.**—In recent wounds of traumatic origin europhen has proved of great usefulness, showing a high efficiency as an antiseptic dressing. Marked drying powers without local irritation and absence of odor are the principal advantage of europhen over iodoform. All kinds of wounds heal quickly under it. It has been used with great success after superficial operations, such as removal of skin tumors, circumcision, and cauterization. In **postoperative fistulæ** it has been found better than iodoform. **Erosions, fissures,**

and **sinuses** may be dusted with euophen and then covered with 10 per cent. euophen gauze.

**Cutaneous Disorders.**—In skin affections of a dry or scaly character euophen is inactive, as might be inferred. In dry eczema, favus, and psoriasis its value is slight. As a dusting-powder in the intertrigo of children it has found great favor. In **pustular eczema**, **folliculitis**, **impetigo**, **suppurating lupus**, and **scrofuloderma** euophen has proved of equal value with iodoform. In **scalds** and **burns** and **erysipelas** it is of considerable service, a dressing of 3 parts of euophen in 7 parts of olive oil being suggested. In **chronic**, **indolent ulcers** and in **leg ulcers** with a surrounding eczematous area euophen soothes the burning and itching, and allays the pain, whereas iodoform is irritating. **Boils** and **carbuncles** are dressed successfully with euophen. In the treatment of tubercular growths euophen is inferior to iodoform.

**Venereal Disorders.**—Euophen is a valuable dressing for **balanitis**, **chancroids**, **suppurating buboes**, and **phagedenic ulcers**, as well as for **tertiary syphilitic conditions affecting mucous surfaces**, or with a moist or secreting surface. Euophen may be applied, as in other surgical cases, in powder, ointment, oily solution, or in the form of gauze, as the nature of the case requires.

**Nasal Disorders.**—In **atrophic rhinitis**, **ozena**, **septal ulceration** (syphilitic or traumatic), and in **postoperative wounds of the nasal cavities** euophen is very valuable, as it adheres well to the mucous membrane, is devoid of unpleasant odor, and has marked antiseptic and healing powers.

**Ophthalmic Disorders.**—Pick (1910) found euophen valuable in **septic diseases of the eye**, particularly when these occur as a result of local injury, foreign bodies, etc. He evacuated the pus and introduced euophen into the organ. W.

**EXALGIN**—Exalgin (methylphenylacetamide, or methylacetanilid) is prepared by warming together monomethylaniline and acetyl chloride. It occurs in acicular needles, which are with difficulty soluble in cold water, more readily in warm

water, and more easily in dilute and concentrated alcohol. It is odorless and tasteless.

**DOSE.**—Exalgin may be given to adults in doses of 2 to 4 grains (0.12 to 0.25 Gm.) every two to four hours. A maximal daily dose of 15 grains (1 Gm.) should not be exceeded. According to Bardet the doses of exalgin, as set forth in the formularies, are too high. The maximum dose for twenty-four hours should be, for a man, 4 grains (0.25 Gm.), and for a woman, 2½ grains (0.16 Gm.). Children from 1 to 12 years of age may be given ½ to 1½ grains (0.032 to 0.1 Gm.) three times daily. Owing to its pleasant taste, it may be given dry on the tongue, in wafers, and dissolved in wine or water, to which a little alcohol has been added (exalgin, 1 part; alcohol, 1¼ parts; sweetened water, 125 parts).

Sodium salicylate added to exalgin increases its solubility for hypodermic use (exalgin, 10 parts; sodium salicylate, 11 parts; water, 100 parts). In short, the dose of exalgin is one-fifth that of antipyrin.

**PHYSIOLOGICAL ACTION.**—This is similar to that of acetanilid. It is capable of acting energetically upon sensibility and the motor-nerve system, and later upon the respiratory and circulatory systems. In tonic doses it acts upon the blood-corpuscles like all poisons of the same class and diminishes the activity of the gaseous changes therein. In animals, mortally toxic doses produce violent convulsions and insensibility; death is from asphyxia. In toxic non-mortal doses convulsions are observed. In man the temperature is not reduced except when exalgin is administered in small, repeated doses during several hours. It acts first upon sensibility; its action upon thermogenesis comes later and is accessory. With feverish patients untoward effects are accentuated; hence the presence of fever is a contraindication to its use. While large doses in animals do not produce albuminuria or hematuria (Brig-onnet), in man the quantity of urine decreases, the color becomes darker, and urobilin and indican are present, if the dose is large. Arterial pressure occasionally falls slightly, though usually



there is a rise, with a decrease in pulse rate. Vasomotor disturbances are indicated by free or profuse diaphoresis.

**EXALGIN POISONING.**—No fatal poisoning from exalgin has been reported, although serious symptoms have followed so small a dose as 5 grains (0.3 Gm.). In this case, an asthmatic, the effects of this small dose were noticed within five minutes. Unconsciousness was associated with shallow, infrequent, and failing respiration. The lips and finger-tips became cyanosed and the extremities cold; the pupils were fixed and widely dilated; knee-jerks were absent. Later an evident tendency to heart-failure. The urine could be drawn with catheter (secretion suppression). In other cases larger doses have produced numbness and tingling, vertigo, temporary blindness, tinnitus aurium, headache, profuse sweating, cyanosis followed by pallor, formication, etc. The brain seems to be the first organ affected and the first to recover. General motor paralysis with dyspnea, pallor, palpitation, and physical prostration were the symptoms in another case. There is sometimes a feeling of alternate expansion and contraction of the head.

Case of an arthritic and hysterical woman, who took, for the mitigation of an attack of migraine, a cachet containing 4 grains (0.25 Gm.) of exalgin. This dose in a short time produced upon the skin and the mucous membrane of the anus and vagina a general papulose eruption, with patches of a fiery-red color, and, in certain spots, large blisters, containing a clear, serous fluid. The rash, which lasted four days, caused pain when pressure was applied, but it was not pruriginous. Linossier (*Jour. de Pharm. et de Chim.*, No. 8, p. 413, 1898).

Case of exalgin poisoning occurring in an adult male Chinaman. It was estimated that the dose taken was 150 grains (5 Gm.) of Merck's preparation. The patient when seen was quite unconscious, intensely livid, with pinpoint pupils and a full, bounding pulse. His temperature was 100.6° F. (38.1° C.). He had vomited once. He was given 30 grains (2

Gm.) of **salicylic acid** by a nasal tube and  $\frac{1}{10}$  grain (0.0013 Gm.) of **atropine** hypodermically, and was put to bed. Two hours later he was given  $\frac{1}{100}$  grain (0.00065 Gm.) of atropine, and a few hours later a third dose consisting of  $\frac{1}{100}$  grain (0.00065 Gm.). The urine contained albumin when first seen, but by the following morning the albumin had disappeared and the patient generally was much improved. Complete recovery ensued. J. Bell (*Lancet*, Sept. 30, 1899).

A patient suffering considerably from headache and insomnia received  $\frac{1}{2}$  Gm. (7½ grains) of the drug in the morning; during the afternoon she complained considerably of palpitation of the heart and a feeling of oppression. After subsequent doses of the same size the distress became even more marked and was coupled with formication, vertigo, spots before the eyes, tinnitus, dilation of the pupils, increased pulse rate, and a pronounced cyanosis of the visible mucous membranes. After two days of active treatment with stimulants, warm baths, and diuretics, the symptoms had disappeared. That great care is to be exercised in the administration of exalgin is evident. O. Seifert (*Wien. klin. Rundsch.*, June 29, 1902).

**Treatment of Exalgin Poisoning.**—The first indication in the treatment of poisoning is to evacuate the stomach. **Apomorphine** in doses of  $\frac{1}{10}$  to  $\frac{1}{6}$  grain (0.006 to 0.01 Gm.) may be given hypodermically for this purpose. Cardiac and respiratory stimulants (**ether**, **strychnine**, and **caffeine** by hypodermic injection, or **strong coffee by the rectum**) are then demanded. **Morphine** by injection may be given if there are convulsions or if much rigidity is present. If the respirations fail, **artificial respiration** should be kept up faithfully, and **faradization of the phrenic nerve**, **stimulants**, and **warmth** applied. In all cases of poisoning thus far reported, these remedies have been successfully used.

**THERAPEUTICS.**—Exalgin is essentially a remedy against pain, as its name

indicates. It is an antineuralgic, antirheumatic, and sedative. It should never be given to patients suffering with any interference of respiration nor used as a means of reducing temperature, for experience has shown that in febrile cases the untoward effects of the drug are marked.

Used externally diluted, as a dusting powder, exalgin has been found to exert a slight anesthetic effect on painful **ulcers**, **burns**, and injured surfaces.

Exalgin is used to relieve the pain of **rheumatism**, **arthritis**, the various forms of **neuralgia**, **headaches**, and the lightning pains of **locomotor ataxia**.

Small night and morning doses (2 or 3 grains—0.12 or 0.2 Gm.) have been found useful in many cases of **epilepsy** and **chorea**, but in these disorders medication must be continued for several weeks to be successful.

In all cases exalgin should be administered in small doses until the susceptibility of the patient is ascertained; thus only will dangerous symptoms be avoided.

W.

## EXOPHTHALMIC GOITER.

See GRAVES'S DISEASE.

**EXTERNAL EAR, DISEASES OF THE.**—The external ear furnishes about one-fourth of all aural work, by reason of its diseases and anomalies; and in consideration of the fact that much of our examination and treatment of the middle ear has to be through this channel, its careful study is requisite in otology. Statistical tables show that more than half of these are cases of impacted cerumen, and the bulk of the remainder fall under the convenient—if vague—headings of diffuse, or eczematous, and circumscribed, or furuncular, inflammations; but the rarer affections have still enough of pathological interest to call for brief discussion.

**MALFORMATIONS.**—Many of the malformations of the auricle have

only embryological interest; but the rudimentary microtia is usually accompanied by stenosis or absence of the auditory canal, and the question of operative intervention comes up,—generally for a negative answer. Possibly a crumpled auricle can be straightened out by plastic operation for more natural growth, and a covered bony canal can be opened; yet too often exploration fails to find the canal, and even the tympanum may be undeveloped; so any opening of the bone is contraindicated. Otherwise any reasonable **plastic surgery** may be attempted. The little *congenital fistula* seen at times above the tragus may suppurate and demand **curetting** or **excision**, and auricular appendages or reduplications of the auricle may call for **removal**. Bad malposition of the auricles may rarely justify **cosmetic operation**.

*Prominent ears*, in addition to being unsightly and a cause of mental suffering to the owner, are a source of physical danger in that they may deflect currents of cold air against a delicate drum membrane, especially on windy days. For this latter reason he suggests the desirability of changing the "set" of them. In his method of operation he excises practically all the fibrocartilage of the concha, antihelix, and antitragus. An ellipse of skin is removed from the posterior part of the ear and from the mastoid region of the scalp, of such a shape that one half relates to the ear and the other half to the mastoid region of the scalp. The cartilage is then removed, and the very thin skin over concha and antihelix is buttonholed at one or more points for purposes of drainage. The ear is then sutured in place, and two thicknesses of iodoform gauze cut to conform with the wound line are nicely fitted between the skin of helix and skin of scalp. Previous to **operation** the auditory canal is plugged with cotton which is

removed, and the meatus left open, before the final dressings of iodoform gauze are applied. Morris (Med. Rec., March 23, 1912).

In congenitally closed external meatus, the writer removes the obstructing tissue, then makes a plug or splint out of a hard preparation of paraffin and wax to fit the orifice and keeps it in place until the skin or mucosa has reformed. The opening is thus maintained without pain or further operative procedure. Stahlman (Penna. Med. Jour., Sept., 1921).

**INJURIES.**—Wounds, burns, frost-bite, and abscesses (see **FURUNCLE**, below) should receive the usual surgical treatment, the last being rare except in the lobule, where generally due to septic piercing for earrings.

Hematoma and perichondritis are often of traumatic origin, each marked by effusion between the perichondrium and cartilage, with serious impairment of its vitality. Deformity is apt to follow; but early relief of tension and judicious use of massage are our best measures for cure or mitigation. Any inflammatory symptoms, such as usually differentiate these otherwise similar affections, are to be allayed before much stimulation is attempted.

Wounds of the auditory apparatus are very frequent in war, being due not alone to direct projectiles but also to the effects of explosions. The author treats especially of stenosis and consecutive atresia of the canal. If after as wide excision as possible of the cicatricial tissue there is still a tendency to re-formation of the stenosis, it will be necessary to: (1) Enlarge the external auditory canal by abrading its posterior wall as far as the tympanic membrane; (2) make an autoplasty of the membranous conduit according to Moure's method in order to obtain as large a meatus as possible; (3) attach great importance

to post-operative dressings. By following such procedure the author has obtained definite recovery in the majority of cases of stenosis. I. Rozier (Rev. de Laryn., xxxviii, 361, 1917).

**GROWTHS.**—Cysts are generally back of the ear and more commonly congenital, however late the apparent beginning. They may be serous, sebaceous, or teratoid, and should be dissected out entire.

Fibroma of the lobule is usually a keloid formation sequent upon piercing or the wearing of irritating rings; it is therefore commoner in the negro. It is not apt to attain great size and seems always benign; but thorough eradication is the only safeguard against prompt recurrence. Other neoplasms, epithelioma in particular, are occasionally observed.

Between seborrhic patches of the auricle and epitheliomas there is no borderline, either pathologically or clinically. Of the writers' 46 cases of epithelioma, most were of the basal-cell type and not very refractory, unless they invaded the external auditory meatus. They may be painful and tender. **X-rays** or **radium** is the treatment of choice, especially the latter. Radium may be used for cross-firing. Any remaining cells of low-grade vitality are best destroyed with **trichloroacetic acid** or **acid nitrate of mercury** and, if necessary, the **curet**. Montgomery and Culver (Arch. of Derm. and Syph., Apr., 1923).

**ECZEMATOUS INFLAMMATION** of the auricle is commonly due to its extension from the canal, where it has been set up by irritating discharges. Intertrigo back of the ear or isolated affection of the pinna or canal has often other causes; and in the absence of otorrhea, gout, struma, or other malnutrition is apt to be its basis. It may be a severe affection,

with pyrexia and almost phlegmonous swelling, and in such cases it is wiser to isolate, give full doses of **tr. ferri chlor.**, and deal with it as erysipelatous. Locally there are generally abundant micro-organisms; and whether these are causative or not, we should, with all promptness, remove the conditions favorable to their growth. Moisture is to be avoided, as well as any oily materials which might decompose and irritate, and any weeping of the surface should be dried by vigorous use of **silver nitrate**. **Bismuth**, **calomel**, **hydrarg. oxidi flavi**, or **ichthyol** in **weak ointment** should relieve the irritable conditions—oil of **cade** or more stimulating salves, the more chronic phases. As a prelude to any treatment, the affected surface should be cleaned as perfectly as possible of all crusts or desquamation, **hydrogen dioxide**, especially in 60 per cent. alcoholic solution, being probably the best agent, since it also penetrates and disinfects, while bringing to view, as snowy patches, affected areas beneath the surface. The chosen ointment should then be rubbed in, gently but persistently, until these deeper patches have been again made invisible by its penetration. The prescribing of medication without supervising or personally carrying out the employment of it will generally prove ineffectual. It is safest to continue its use periodically for a month after all symptoms are past.

Eczema of the external ear is often stubborn at best and prone to recur, and **strict regimen** and constitutional medication may be requisite to ward off attacks. Herpes may, in very rare cases, be mistaken for it; but the pain in herpes is very apt to be severe before any eruption occurs, and the

course of the affection is quite different.

The itching of eczema is as trying in the canal as in any other location, and there is a strong temptation to scratch, abrade, and infect the surfaces. Furuncle is apt to follow, and autoinoculation may establish a series. As elsewhere, there are two sets of glands open to involvement, the superficial sebaceous hair-glands and the deeper coiled glands, here secreting cerumen instead of sweat. The latter



Fibrous tumors of the lobules. (Bullard.)

may actually enter the perichondrium or periosteum; so their suppuration may not only cause swelling of the whole aural region and displace the auricle in a way suggestive of mastoid abscess, but may really cause caries of the bony wall. Hence slight eczemas deserve treatment as a prophylaxis, even when no redness or desquamation marks their existence.

Induration is present in most chronic eczemas, and the resulting rigidity of the auricle and canal is often our only diagnostic sign. Something of this sort will generally be found in the other ear when one only is affected with furuncle. The right

ear is more often affected in adults, probably as it is more often scratched.

In eczema of the auricle, the writer advises **protective ointments** early, and later cleaning off of the crusts and **stimulating ointments**, **X-ray** treatment and injections of **sodium cacodylate**; **mesothorium**, **bromide**, and **urotropin** are also recommended. The prognosis depends on the underlying cause. A good drying powder consists of **talcum**, 25 parts; **zinc oxide**, 5, and **starch**, 100. De Carvalho (Brazil-med., Jan. 22, 1921).

**FURUNCLE** may be extremely painful and a series occurring in a patient out of health may positively endanger life through exhaustion. The first appearances should be vigorously treated, therefore, and the later stages sedulously cared for until resolution is complete.

The hearing is unlikely to be involved except temporarily; but the condition should not be too lightly regarded or the sufferer may seek a more sympathetic attendant. **Leeching** may greatly relieve the painful tension and abort or limit the lesion; **heat**, dry or by douche, is generally more convenient and as efficacious. The temperature should always be hotter than pleasant and the douche should be followed by drying, to avoid maceration. Poulticing is to be condemned, unless done for very brief intervals and only at the hottest bearable. Granulations about the mouth of an open furuncle are almost as certain evidence of abuse of poultices as is a "tea-leaf eye." Disinfection by mopping with **hydrogen peroxide** gives the benefit of massage, and should be followed by rubbing in of the **ointment of the yellow oxide of mercury**. This should not only be rubbed in vigorously, but be inserted

on a conical wad of cotton wedged in as firmly as can be tolerated. If the patient will bear this for the first few minutes, it generally reduces the congestion and brings relief, and it can even be pushed in more and more so as to maintain pressure. A persistent inunction and massage are thus obtained at every motion of the jaw, and a canal that was wholly closed one day with a furuncle that threatened days of suffering may be found open and well on toward resolution next day. In the deeper form of the involvement such pressure cannot be endured. Heat will here have a limited value, and instillations of atropine, cocaine, morphine, carbolic acid, or a thousand vaunted remedies may avail as little. **Morphine** in full dose must be called in, therefore, to supplement the resolvent effect of **heat** by douche and hot-water bottle. Bags of salt retain heat well and can be used to good advantage, as can the Japanese hand-stove if its fumes are avoided. **Incision** of the swelled tissue, whether pus has formed or not, is in theory unimpeachable; in practice it can be generally avoided with moral and physical relief to the patient and an impression that the healing has been better without it. Diagnosis of the conditions beyond the swelling may be impossible, and tympanic involvement had better be assumed until it can be disproved; hence swellings in the bony canal, where glands are few and furuncle rare, should be earlier incised, and the possibility of underlying bone disease never lost sight of as a cause, rather than a consequence, of the visible lesion.

Six cases in which circumscribed otitis in the outer ear was treated in-

ternally with **yeast**, taken two, three, and four times a day. The tendency to recurring furuncles in the ear was promptly arrested and there has been no recurrence since. The patients took the yeast for about a week. This yeast treatment was supplemented by local application of medicated gauze. Under the influence of the yeast the pain and the morbid tendency rapidly subsided, although the furunculosis had long persisted unmodified by other measures. N. Antenore (*Gazz. degli Ospedali e delle Clin.*, May 4, 1909).

A small pledget of cotton-wool is impregnated with equal quantities of **ichthylol** and **glycerin** and introduced into the meatus, followed by a second pledget of dry cotton-wool to prevent any of the solution running out. Care must be taken to prevent the pledgets from exercising any pressure, otherwise the pain would be increased. The application may be renewed once a day, or in very painful cases night and morning, and the treatment should be continued until the desiccation of the furuncle is complete. If the furuncle breaks, the cotton-wool impregnated with ichthylol prevents further infection of the meatus inward, and there is no fear of setting up eczema of the passage, such as not infrequently occurs with other moist applications or instillations of glycerin and carbolic. In cases in which it may be necessary to incise the furuncle the ichthylol application forms a suitable subsequent dressing. F. Bruch (*Merck's Archives*, March, 1910).

In acute otitis media and the extremely painful furunculosis of the auditory meatus, the writer recommends the following combination:—

R *Æthylis amino-*  
*benzoatis* ... 1 Gm. (15 grains).  
*Alcohol absol.* . 10 Gm. (2½ drams).  
*Liq. alum. acet-*  
*tatis* ..... 2 Gm. (30 minims).  
*Glycerini* ..... 30 Gm. (1 ounce).

The solution is warmed and applied by saturating with it a sterile strip of gauze which is inserted up to the drum membrane three to five times a day.

The gauze is then moistened with the solution, while externally a Priessnitz dressing is applied.

The above formula or combination is very effectual and never causes any intoxication like cocaine or any cauterization like the popular 10 per cent. carbolyzed glycerin.

For painful affections of the larynx, the author prefers a mixture of equal parts of ethyl aminobenzoate (anesthesin) and iodol with 1 per cent. menthol, insufflated three times a day. Huebner (*Therap. Monats.*, Feb., 1912).

During the preparation of the **autogenous vaccine**, which takes 2 days, the writer frequently gives an initial dose of a pure staphylococcus aureus or albus vaccine, prepared and kept on hand in the laboratory. If the offending organism corresponds to the organism of the vaccine used in the first treatment, and if there has been an improvement, the stock vaccine is continued; in other circumstances the autogenous preparation is substituted. II. Beattie Brown (*Annals of Otol., Rhin. and Larynx.*, Sept., 1914).

The writer finds that **heat** may effect a cure in mild cases. Where there is pus, he makes deep **incisions**, and 24 hours later inserts a gauze strip soaked in **aluminum subacetate** solution, to be kept moist by the patient with a medicine dropper. Prehn (*Boston Med. and Surg. Jour.*, Oct. 14, 1920).

**GRANULATION MASSES** may be found in the canal, arising from its wall. Unless fringing the opening of a poulticed furuncle, these generally mark a sinus leading to or into the bone. There may be a burrowing out of tympanic pus along the periosteum by a track which a bristle could hardly follow; but generally a fine probe will find its way to bare and carious bone. A superficial lesion should be laid open and **curetted**, as **cocaine** will generally enable us to do with sufficient

vigor. A deeper lesion will belong to the field of middle-ear surgery.

**INSPISSATED CERUMEN** constitutes about one-seventh of the aural disorders. It is rarely a condition that can be regarded as merely an incidental retention of normal earwax, nor does the dirty occupation of even the coal-heavers, who are affected with it, more than partially explain its occurrence. There is generally more or less involvement of the middle ear behind it, and the *decreased* amount and greater consistence of the excretion is often, as in the pharynx, the reason for the apparent increase of its amount. Wax is generally wholly lacking in suppurating ears, although brownish, inspissated pus is easily mistaken for it; and in the chronic tympanic catarrhs it is generally a very good omen when wax begins again to form in the usually empty canal. Faulty configuration sometimes hinders its natural escape; but generally this is associated with an eczema which adds much exfoliated epidermis to the collection. The wax glands are situated only in the outer two-thirds of the canal; so any wax found deeper is a foreign body, generally pushed there by meddlesome attempts at its removal.

The healthy ear needs no artificial cleansing of its canal. Nature has provided that the epithelium of the center of the drumhead shall grow faster than at any other point; hence it tends to overgrow its surroundings, as it were, and, pushing the older cells before it, to creep along the canal wall. Superficial extravasations on the drumhead can thus be seen to migrate off its surface and a little way along the canal, before they are thrown off; and this outward growth carries all foreign material away from the tympanic membrane, where it might seriously impede func-

tion. Outside of the narrowed "isthmus" of the canal the wax glands are present, and one of the functions of the wax is doubtless to agglutinate the flaky material. The motions imparted by the jaw to the lining of the canal are then probably all that is needful to convey these particles to the exit,—the spring of the hairs upon which they get caught serving to throw them at times out upon the shoulder.

When, through defect of this natural cleansing process or artificial interference with it, collections form within the canal, they are commonly at the middle third and may fill almost completely this tube; but so long as the smallest crevice remains through which the sound-waves can reach the tympanum there may be no symptom of their presence. Pressure may be noted or other irritation lead to interference, and then the mass may be pushed down upon the drum or made to occlude the meatus. More often the entrance of moisture swells the hygroscopic mass, and sudden and complete closure of the ear, with deafness, tinnitus, and autophony, may alarm as well as distress the patient. Sudden deafness without pain or vertigo is apt to signify impacted cerumen.

The opposite ear is commonly in similar condition; so the habit of examining it first may save us from letting the same experience befall the patient there. A dark-brown or blackish, greasy mass can usually be seen at the first glance, even on drawing the canal straight and letting the light from a window fall into it past the examiner's head. Sometimes the hairs are enough to hide it and must be pressed aside with a speculum. This must here, as always, be used only under good illumination of the canal or it may serve to press the mass all the more distressingly. In all these exami-

nations, as also in all manipulations in the canal, the normal configuration of the meatus must be borne in mind. It has an oval lumen with the longer diameter vertical at the exit, but inclining forward as we go in. Its axis is spirally curved and tends usually upward and forward as we pass in, but the floor seems to sink a little as we approach the drumhead, constituting a slightly broadened, deepened sulcus, out of which foreign materials are rather hard to remove. The soft parts constituting the outermost third of the canal exaggerate the curves and have to be drawn up (down, in the infant) and back and out in order to straighten it as much as possible, both for seeing in and for washing out anything there retained. The helix should therefore always be grasped between the index and middle fingers, so that this traction may be efficiently made, and yet the thumb and index tip be left free to manipulate a speculum or otherwise serve us.

Wax plugs and all other foreign bodies should be washed out with the **syringe**. Only where this has been fully and skillfully used without avail has the most expert a right to employ other instruments, and then only with a gentle, steady hand and on a quiet or etherized patient. In almost all cases the syringe is the most efficient as well as the safest and gentlest means at our command; but it must be better used than is common if it is to justify this claim. A small, smoothly working piston syringe is to be preferred, with a small tip that can enter a little way into the canal without obstructing the view. The fluid employed should be **hot water**. It matters little or not at all whether this is medicated; **soda**, **boric acid**, or any harmless drug may be dissolved in it if the surgeon believes it better than pure

water. The best solvent is really heat, and a temperature of 110° to 115° F. (43.3° to 46.1° C.) is generally well borne and less apt to cause dizziness than "lukewarm" water. A cup of some sort should be held beneath the lobule and the shoulder covered with a towel; then with the canal well illuminated by the forehead mirror or other means and drawn straight as above described, we gently begin to inject the hot water. Perhaps along the upper back wall is the best direction for the stream; but this must be varied as sight of the mass suggests. Beginning gently, the first few drams serve to moisten the parts, the next to disintegrate the plug, discoloring the returning fluid with the dissolved wax; usually with my two-dram instrument the eighth syringe-ful washes the mass out into the cup, with an expenditure of 2 ounces (60c.c.) of water and five minutes, at most, of time.

But epidermis is not soluble in water or any other available material. When the impaction consists largely of laminated epithelium, especially if really a cholesteatoma mass working out from the middle ear, no such easy task is to be anticipated. Prolonged syringing, aided by skillful use of the probe and forceps, perhaps, must be employed to remove such a mass, and prudence may dictate adjourning the completion of the matter to a second sitting. The canal walls are often excoriated beneath such a mass, and exfoliating, but not yet fully detached, epidermis may anchor it to tender surfaces, from which it should not be violently torn away. But in true cerumen impaction there is little or none of this. Delay in soaking or otherwise trifling with the plug only increases any irritation from its pressure. The patient, if put off, may never



return to the surgeon, whom he truly says made him worse instead of better. *Dizziness* or *fainting* may compel a suspension of the sitting; but if the patient has been warned to announce the first sensation of the sort, this can generally be forestalled, and an eye should generally be kept open for any clammy sweat on his brow. Pressure upon the tympanic structures is a common cause, and suction with the squeezed Politzer bag fitted in the canal or the palm laid over the ear will often undo the mischief and give instant relief. If not, the patient should be laid flat by tilting his chair back until the head is on or near the floor and be induced to lie still until feeling right again, when the chair can be raised again and we can proceed in a few moments without repetition of the disturbance.

After this and all other syringing, the canal should be gently dried with absorbent cotton on a delicate carrier and the air shut out by a light flake in the exit; otherwise there will be chilling from the evaporation of the trace of moisture left, with possibly unpleasant reaction. Any *excoriated surfaces* should be anointed or dusted with **boric acid** or **aristol**, and any needed treatment given to the nose, throat, and middle ear.

**FOREIGN BODIES** in the ear are not common or important except as furnishing to incompetent and rash attendants opportunity for improper and sometimes most **injurious interference**. This should be carefully **avoided**. Let alone, none but gunshot missiles or living insects can often occasion the slightest damage, except as forming nuclei for subsequent collections of cerumen.

It is the injury inflicted in efforts to remove them that is responsible

for numerous untoward results, occasionally fatal. Rarely will any such object be thrust primarily beyond the cartilaginous portion of the canal, whence its extraction by any competent method should be easy. It is only after family or friend or incompetent medical man has pressed it deeper, and too often wounded or irritated to marked swelling the tissues about it, that the condition assumes any importance. Then the panic which assumes that it "will certainly go to the brain" must first be allayed; the patient quieted to bear examination, which previous abuse has taught him to dread, and the ground clearly taken that the intruding mass will be at once removed only if this can be safely done. To counsel delay *after* failure is apt to seem a reason for immediately seeking another and more vigorous attendant. Careful examination should first be made to determine the presence of the alleged foreign body, and this should begin with the other ear, not only that the configuration of the parts may be noted, but because in the excitement one ear may be receiving attention belonging to both or to the other alone. If there is, in fact, a body to be removed, the **syringe** and **water of about 105° F.** (40.5° C.) should be used as above directed, and, unless there has been very bad mishandling, there is likely to be little difficulty in washing out the intruder.

Should there be firm impaction in the bony canal or such swelling of the soft parts as to defy this procedure, it is best to use the water hotter still to reduce the inflammation and then to wait until the conditions are more favorable. Urgent symptoms may forbid this delay; then if vigorous syringing is unavailing, other instruments, such as a

fine loop of wire or a blunt hook, may be tried in skillful hands, usually under general anesthesia, unless the patient is in perfect control. All but **specially adapted forceps** are commonly worse than useless and apt to force the body deeper. The **agglutination method** may suit those who fear to use water lest it swell some bodies and cause seeds to germinate before they can be removed; but hours can rarely be spent over such matters. If the body really needs removal it is safer to lay the soft parts forward by a free **incision** behind the auricle, and in the shorter and wider naked canal to use efficient leverage or bold chiseling to free and extract the mass. The injury thus surgically inflicted should be healed in a week; what will be done in blindly groping in the depths of the ear may never be repaired, and the life as well as the hearing may be sacrificed by such "conservatism."

If after syringing vainly an impacted seed it is decided to wait for reduced inflammation, a few drops of **carbulated glycerin** will serve as a sedative astringent and will dehydrate the seed as much as hours of syringing could swell it. So the science of those who syringe with substitutes for water is as wasted as that which floated up leaden shot with mercury instead of turning the ear down to let them fall out. **Gravity** can often be utilized in thus inclining the head, and **gentle rotary rubbing** in front of the ear will often coax out the foreign body. An **air-douche** with the Politzer bag or other means will sometimes best remove light substances, proving as efficacious as the old-fashioned, but reprehensible, "box on the ear" which has sent many a cherry-stone or pebble flying out across the

room. The ear should be directed downward, drawn straight, and relieved of any pressure of the jaw-condyle by opening the mouth.

**OTOMYCOSIS**, or the growth of aspergillus or other molds in the auditory canal, is a rare affection, practically an eczematous inflammation with this infection as an accidental sequence and persisting irritant. Such organisms cannot flourish in a dry ear. It should be well cleansed and rigorously mopped with **hydrogen dioxide**, best that containing 60 per cent. alcohol, then dried with all thoroughness, and dusted with **boric acid**. Instillation of **borated alcohol** may precede this last, if it does not irritate too much. In the very rare instances when a few repetitions of this procedure fail of complete success, some of the many other commended drugs may be tried. As the growth may have penetrated deeply into the epithelium, no single treatment can be trusted to have destroyed every hypha and spore, and a non-mycotic eczema may remain to be cured, and here **silver nitrate** is often our best antiseptic and astringent.

To extract a foreign body, the writer inserts into the canal 1 or 2 small gauze drains, pours into the canal melted **ambrine**, and applies a cold compress. Traction on the gauze then brings out the ambrine with the foreign body embedded in it. De Kerangel (Rev. de laryn., iv, 145, 1922).

**HYPEROSTOSIS**.—Exostosis and hyperostosis are generally self-limiting affections, very rarely in America calling for operation, but sometimes due to a hidden suppuration which they seriously complicate, and other new growths are too infrequent to call for special discussion.

B. ALEXANDER RANDALL,  
Philadelphia.

**EYELIDS, DISEASES OF THE.**  
**—INFLAMMATION OF THE**  
**EYELIDS.** (See BLEPHARITIS, volume i.)

**INJURIES OF THE EYELIDS.**

The lids may be the seat of all kinds of injuries, and, on account of the looseness of the skin over the overlying tissues, edema and ecchymosis are usually present.

Abscesses of the lid give rise to a localized red swelling, associated with more or less edema and hyperemia of the entire lid and the conjunctiva lining it. Throbbing pain in the eye and head and some fever accompany its formation. Abscess of the lid is usually the result of traumatism, but may be secondary to periostitis or caries of the margin of the orbit.

**Treatment.**—If there be a solution in the continuity of the lid, the edges of the wound should be carefully approximated with **sutures** and evaporating lotions, like dilute **lead water** and **laudanum**, should be applied. Simple *ecchymosis* of the lids, usually designated as "black eye," should be treated with **ice-compresses** and **lead water** and **laudanum**. When an *abscess* is present, **hot fomentations** are useful until fluctuation is detected. An **incision** should then be made into the abscess parallel to the muscle-fibers.

**HORDEOLUM (STYE).**—Hordeolum is a circumscribed purulent inflammation situated at the follicle of an eyelash. At first there is a hard swelling, with more or less involvement of the entire lid. A yellow head soon caps the little tumor, and, if allowed to go on, this will break open and the contents be discharged. There is usually a feeling of great tension in the lid until the abscess is opened,

and there may be slight febrile disturbance.

Hordeolum is found chiefly in the young, especially in anemic girls, where it is the expression of a constitutional disturbance. Habitual constipation has been assigned as a common source of the inflammation. When associated with boils, etc., the urine should be tested for sugar, especially in adults. Uncorrected ametropia is a frequent cause.

**Treatment.**—The inflammation may at times be aborted in the earliest stages by **hot boric lotion**, by **massage** with **yellow oxide of mercury**, by applications of **silver nitrate**, or by painting the swelling with **collodion**. If this fails, suppuration should be encouraged by **hot applications**, and a free **incision** be made as soon as pus is suspected. **Sulphide of calcium** internally is frequently of service. The opsonic index of the blood against staphylococci may be taken. It will often be found abnormally low; in these cases **staphylococcic vaccines** should be tried.

**Suction hyperemia** for styes and furuncles of the lids may be applied by means of a rubber ball and glass cups. Hoppe (Munch. med. Woch. Nu. 40, 1906).

The writer has found the most satisfactory treatment to be the following: With a small pair of forceps pull out each hair which shows a collection of pus, or even a red spot, at its root. Direct the patient to apply from ten to thirty times a day a collyrium prepared as described later. If examined again in a few days, the inflammation as a rule will have ceased; but if any pustule is then seen, immediately pull out the eyelash, and continue the applications as before. Ordinarily, everything will have been finished in three or four weeks, and new hairs will rapidly

take the place of those epilated. The remedy used is a combination of astringents, known formerly as *lapis divinus*. The formula, given by Sabouraud, is:—

℞ *Potassium nitrate*,  
*Copper sulphate*,  
*Alum* .....āā 100 Gm. (3½ ounces).  
*Camphor* .... 5 Gm. (1¼ drams).

M. Form into pencils.

A solution of this may be made with rose water of the strength of ½ per cent. Sabouraud (La Clinique, June 14, 1907).

During the acute stages **hot applications** are advised. As soon as the acute stage has somewhat subsided, the writer applies locally:—

℞ *Tinctura arnica* ..... 16 Gm. (3ss).  
*Tinctura opii*,  
*Liquoris plumbi sub-*  
*acetatis dil.* .....āā 8 Gm. (3ij).  
*Aquæ destil.*, q.s. ad. . 90 Gm. (3iij).

M. Sig.: Apply locally by means of absorbent cotton at bedtime.

After the disappearance of the stye for a period of four weeks, the following ointment is employed:—

℞ *Hydrargyri*  
*chloridi cor-*  
*rosivi* ..... 0.008 Gm. (gr. ⅙).  
*Petrolati albi* .. 8.0 Gm. (3ij).

M. Sig.: Externally.

This should not be merely smeared over the lids, but be applied with gentle massage every night. Prior to the application of this antiseptic ointment hot compresses should be applied to stimulate the circulation of the margin of the lids. Brav (N. Y. Med. Jour., Sept. 18, 1909).

The writer recommends treatment with **vaccines** in preventing relapses of stye. He uses preferably a stock **staphylococcus vaccine**, as an autogenous vaccine can be obtained only after 3 or 4 days. Two or 3 injections are administered, 1 every third day. In 18 cases out of 20 the folliculitis of the lid disappeared, while in 2 instances relapses have persisted. G. Cousin (Paris méd., Sept. 6, 1924).

**CHALAZION.**—Chalazion is a hard swelling which forms in the lids in connection with a Meibomian gland. It varies in size from the head of a pin to a large pea. Suppuration may occur, and the viscid contents of the tumor be discharged on the conjunctival surface of the lid, or the growth may be wholly absorbed and disappear. As a rule, it causes but little pain; rarely, however, it takes an acute form, when the symptoms resemble those of hordeolum.

Chalazion originates in a chronic inflammatory process in the connective tissue surrounding a Meibomian gland, especially where there is uncorrected ametropia. The condition usually occurs in adults.

**Treatment** may be either abortive or radical. The former is rarely successful, but **massage** of the growth may be tried, using an ointment of **yellow oxide of mercury** or **iodide of cadmium**.

The radical plan consists in the **removal of the growth by operation**, either from the skin or conjunctival surfaces. If the tumor shows evidence of having broken down, it had better be removed from the latter surface. This is accomplished by means of a vertical incision into the growth with a sharp scalpel, after thorough cocaineization of the conjunctiva, and the removal of the contents of the sac with a small curette or scoop especially constructed for this purpose. If, on the other hand, the growth is large and firm, and gives no evidence of having undergone degeneration, it is better to remove it from the skin-surface by means of a formal dissection. For this purpose it is customary to control the hemorrhage by means of a clamp which includes the field of

operation in its area, and to insert several stitches after the tumor has been excised. Care should be taken that all of the growth be removed.

The writer first **removes** part of the covering of the chalazion with scissors. A 10 per cent. solution of **cocaine** is rubbed well into the everted lids, and the incision made converted into a triangular opening by means of scissors. Cocaine solution is then applied in the cavity, the contents curetted, and the cavity cauterized with **trichloroacetic acid**. After irrigation with **sodium bicarbonate** solution, **hot, moist cloths** are applied. Wickliffe (Ky. Med. Jour., Aug., 1914).

The important thing in the **incision** and **curetting** of a Meibomian cyst is to split the cyst from its conjunctival surface in the long axis of the gland to and through its opening on the free border of the lid. John Dunn (Arch. of Ophthal., Jan., 1919).

## CUTANEOUS DISORDERS OF THE EYELIDS.

**ECZEMA.**—Eczema is one of the most frequent of palpebral affections; it is usually met with in children in its moist form (*crusta lactea*). It is generally secondary to phlyctenular conjunctivitis, and results from the continued irritation of the lids by the profuse lachrymation incident upon this form of conjunctivitis. A similar eruption is seen in adults, especially in the lower lid, when the lachrymation is secondary to lachrymal disease or catarrh of the conjunctiva.

**Treatment.**—Removal of the scabs with a warm solution of **bicarbonate of potassium** without provoking any bleeding is advisable. After the lids have been thoroughly dried, a solution of **silver nitrate**, 20 grains (1.3 Gm.) to the ounce (30 Gm.), should be carefully applied to the raw surfaces. The lid should then be covered

with an **oxide of zinc** ointment. Either the plain ointment may be employed or one consisting of equal parts of oxide of zinc and vaselin to which 20 grains (1.3 Gm.) of **calomel** have been added. A mixture of **tragacanth**, 5; **glycerin**, 2; *aquæ dest.*, ad 100, is of service in the treatment of fissures on the angles of the lids in scaly and moist eczemas of the latter.

**HERPES ZOSTER OPHTHALMICUS** is an inflammatory affection of the skin, characterized by the formation of vesicles along the terminal expansions of the supraorbital division of the fifth nerve, and sometimes its nasal branch, and more rarely the infraorbital division of the same nerve as well. The vesicles are generally grouped together and have an inflamed base. At first they contain a limpid fluid, but this soon becomes clouded; the vesicles then dry up and form scabs, which fall off and leave deeply pitted scars that persist during the remainder of life. As a rule, the appearance of the vesicles is preceded by severe neuralgic pain in the course of the affected nerve-branches, and there is some fever. The pain generally subsides with the efflorescence of the vesicles. The eyeball is sometimes implicated, either in the form of a keratitis, iritis, or iridocyclitis. Although the intraocular tension is not infrequently somewhat diminished in the early stage, I have noted the occurrence of the disease with acute glaucoma.

It usually occurs in the old and feeble, although it has been seen in young and healthy individuals.

**Treatment** is wholly symptomatic, and consists in sedative local applications of **lead water** and **laudanum**, or

in dusting **rice starch** over the affected areas. **Morphine** should be administered internally for the relief of pain, and tonics should be directed toward building up the system. For the severe neuralgia which frequently remains after the subsidence of the inflammation, **croton-chloral hydrate**, in doses from 5 to 10 grains (0.3 to 0.6 Gm.) every four hours, and the use of a mild **galvanic current** have been highly recommended. Any ocular involvement must be combated by the proper remedies. The affected eye should be protected by a bandage.

### TUMORS OF THE EYELIDS.

**CARCINOMA** of the eyelids takes the form of *rodent* or *Jacob's ulcer*, occurring in adults, and characterized by a slowly progressive, but destructive, ulcerative process, by which the lids and the neighboring tissues are gradually consumed. The first appearance is that of a pimple, usually at the inner canthus, which becomes indurated and covered by a scab.

**Treatment** should consist in the early and complete removal of all the diseased tissue by **dissection**, followed in some cases by the application of **chloride of zinc** or even of the **actual cautery**. Considerable improvement and even cure have followed the use of **radium**, and this plan of treatment may be essayed for a time in cases where the rodent ulcer has destroyed much tissue.

**XANTHELASMA**.—Xanthelasma are yellowish or buff-colored *plaques*, which are occasionally found upon the eyelids. These patches are slightly raised above the surrounding skin, and are frequently semicircular in shape. They are often symmetrical, and have a predilection for the inner part of the

upper lids. They are more common in women than in men, and occur in adult life as a result of hypertrophy of the sebaceous glands, with subsequent fatty degeneration of the subcutaneous connective tissue.

**Treatment**.—As these growths have no significance other than a cosmetic one, they should not be interfered with, save when they are large and disfiguring, in which event they may be removed by careful **dissection**, or by **electrolysis**.

Palpebral tumors may also be made to disappear by repeated applications of a solution of **monochloracetic acid**.

### MOLLUSCUM CONTAGIOSUM.

—This consists in a white tumor, varying in size from the head of a pin to that of a pea, that forms in the skin of the lid. The disease begins in a sebaceous gland, and is found chiefly among badly nourished children.

**Treatment**.—Treatment consists in **incision** and touching the interior of the growth with solid **nitrate of silver** stick after squeezing out its contents.

**PAPILLOMATA, SARCOMATA, AND EPITHELIOMATA** are all found on the lids, but, as they have no characteristics different from those which they possess elsewhere, do not require detailed study.

Remarkable case in which a large epithelioma beginning at the margin of the lower lid and extending across the entire cornea completely concealed it with, of course, a total blindness of the eye. Immediately upon striking his head accidentally against a tree the affected eye received a violent contusion with profuse hemorrhage. When this was arrested the man found that he had recovered his sight. The cornea was found entirely uncovered and intact and the

remains of the tumor formed a thick fringe about the lower border on the nasal side. Instead of forming an integral part of the cornea the tumor was evidently simply superimposed upon that membrane, which retained its transparency intact.

A few similar cases have been previously reported. It may therefore be advisable, in tumor of the anterior segment of the eyeball, to make a careful dissection to determine the condition of the subjacent cornea. Dujardin (*Clin. Ophth.*, No. 8, p. 119, 1908).

Case of melanotic sarcoma of the tarsal conjunctiva successfully removed, the patient being a man aged 60, and a case of subcutaneous leuko-sarcoma of the upper lid of a boy, aged 5. In this latter case the sarcoma continued its fatal course, notwithstanding 2 operations and roentgen-ray and radium treatment in the course of about 18 months. Satanowsky (*Semana médica*, July 23, 1925).

### HEMANGIOMATA, OR NEVI,

occur on the lids in two forms: telangiectases and cavernous hemangioma. The former are composed of dilated capillaries and take the form of small, bright-red or port-wine colored spots; the latter consists of dilated and anastomosing venous spaces in the subcutaneous tissue. They appear as small, bluish tumors, and increase in size on crying and lowering the head.

**Treatment.**—Both forms may be removed by **electrolysis** or by application of **carbonic acid snow**.

### SYPHILIS OF THE EYELIDS.

Primary sores are found on the margin of the lids, usually at the canthi. The first appearance is that of a pimple, which gradually breaks down into a depressed ulcer, with a characteristic induration of the base. The glands in front of the ear and at the angle of the jaws are almost always involved, and

the usual constitutional signs of syphilis follow. The contagion is carried to the eye, as a rule, by the finger, though in some instances it has followed a kiss or the filthy custom, practised in some communities, of attempting to dislodge foreign bodies from the eye by the tongue.

Rarer forms which occur in the secondary and tertiary stage of the disease consist in a marked induration and swelling of the entire lid, followed by ulceration of the margins of the lids and the loss of the cilia. Syphilis of the lids must be diagnosed from suppurating styes and chalazia, from lupus vulgaris, and from chronic cases of dacryocystitis.

**Treatment.**—Chancres should be dusted with finely powdered **iodide of mercury**, or application made to them with the **black or yellow wash**. General mercurial treatment or **arsphenamin** should be employed as soon as the diagnosis of syphilis is made.

### NEUROSES OF THE EYELIDS.

**BLEPHAROSPASM** is an involuntary contraction of the orbicularis palpebrarum, and may be either the result of irritation of the ophthalmic division of the fifth nerve by reflex action, as in disease of the cornea, etc., or it may be an essential spasm, occurring in eyes that are perfectly normal. A slight twitching in a few fibers of the muscle is not unusual in ametropia and may be made to disappear by the adjustment of the proper glasses.

**Treatment** should aim at the cause. In severe cases hypodermic injections of **morphine** into the lids may be necessary, or even **subcutaneous division of the nerve**.

The writers have successfully practised **section of the facial nerve**, followed by immediate anastomosis with

the eleventh pair in a severe case of this affection, which had been rebellious to both medical and surgical attempts at cure. Section of the facial nerve is followed by a temporary paralysis; the latter soon disappears. Abadie and Cunéo (*Arch. d'oph.*, April, 1905).

**Injections of 80 per cent. alcohol** combined with cocaine or stovaine are a safe, simple, and effective means of treatment of obstinate facial spasm. The treatment is applicable both in simple spasm and in the complicated facial tic douloureux. The injections should be made at the point of emergence of the facial nerve. The paralysis which follows the injections should cause no anxiety, no matter how long it lasts, so long as there is no tendency to alteration of the cornea and the eyes close sufficiently during sleep. Valude (*Tribune méd.*, vol. xli, p. 232, 1908).

The writer makes subcutaneous injections of alcohol (30 parts of absolute alcohol to 60 of sterilized water) superficially in the neighborhood of the stylomastoid foramen under the skin, in the region of the supraorbital nerve and of its palpebral filaments, and in the distribution of the orbital filaments of the facial so as to affect the orbicularis; the injection is administered without an anesthetic. Several injections may be given at daily intervals. Fumagalli (*Annali di oftal.*, vol. xxviii, fasc. 3, p. 162, 1909).

In a case of idiopathic blepharospasm, the writer injected drop by drop, into the inferior external margin of orbit, 2 c.c. ( $\frac{1}{2}$  dram) of a 50 per cent. solution of alcohol, after anesthetizing the area 10 minutes earlier with an equal quantity of a 2 per cent. solution of procaine, injected into the nerve fibers of the orbicularis muscle. The blepharospasm was still absent 3 months later. Van Lint (*Arch. d'ophthal.*, Oct., 1921).

**PTOSIS** is a drooping of the upper lid over the eyeball, with inability to raise the same. When not congenital,

or the result of thickening of the lid from inflammation, it is due to paralysis of that branch of the third nerve which supplies the levator palpebræ superioris. Ptosis is frequently associated with palsies of other muscles supplied by the third nerve, and when it is an isolated symptom suggests central disease.

**Treatment.**—If of recent origin, alteratives, such as mercury and potassium iodides, should be administered in high doses; if of long standing, recourse must be had to operative procedure. That of Panas is preferred. This operation has for its object the securing of a connection between the lid and the frontalis muscle by means of a skin-flap. This flap is obtained by inserting a horn spatula under the upper lid, and by making a horizontal incision about 5 mm. above the margin of the lid through the skin and subcutaneous tissue; another incision, parallel to this and about 1 mm. long, is made through the eyebrow, and is extended as far as the periosteum. Two incisions are then made at right angles to the first inferiorly; the flap of the skin remaining between the two primary incisions is undermined, and the tongue of skin drawn up under the bridge and held in position there by sutures.

A somewhat more recent procedure introduced by Motais has come into favor, and consists essentially in making the superior rectus muscle available for replacing the levator.

The writer speaks favorably of Motais's operation, which consists in the transplantation of the middle portion of the insertion of the superior rectus to the upper margin of the tarsal cartilage. He has performed it on five patients. In the majority the effect was insufficient; so in two the operation was supplemented by



the excision of a strip of tissue, 3 to 4 mm. wide, involving the entire breadth and thickness of the lid. In all a slight degree of lagophthalmos was produced, requiring a strong innervation of the orbicularis to close the lids. Otherwise the cosmetic and optic effect was excellent. A. Elschmig (Med. Klinik, May 15, 1910).

**LAGOPHTHALMOS.**—By this term is meant an inability to close the eyelids. It is either due to paralysis of the facial nerve or is the result of some condition within the orbit, or in the eyeball itself, which causes the globe to protrude between the lids. As a result of the exposure to which the cornea is subjected, it frequently ulcerates, and, unless proper procedures be inaugurated, the eye is lost.

**Treatment.**—If due to paralysis of the seventh nerve, the cornea should be protected by carefully bandaging the eye during sleep, and by cleansing the conjunctival *cul-de-sac* with frequent washings of boric acid solution. The primary cause of the paralysis must be treated, and galvanism and hypodermic injections of strychnine may be tried. If the degree of lagophthalmos be excessive, the bandage should be worn constantly, and at times tarsorrhaphy is necessitated. This operation consists in uniting the margins of the lids by means of sutures after their skin has been removed from the ciliary border by a sharp knife.

### CONGENITAL ANOMALIES OF THE EYELIDS.

Absence of a part of or all of an eyelid or of both eyelids has been noted, though very rarely. *Cleft eyelid*, or *coloboma* of the lid, has also been observed—usually in the upper lid. At times this deformity occurs on both sides.

Case of congenital coloboma of the left upper lid met with in a child  $2\frac{1}{2}$  years old. The defect was triangular with its base at the ciliary margin, its apex about the middle of the lid. The margins of the coloboma were not provided with lashes. The fissure was closed by means of a plastic operation. The writer says that only 80 or 90 similar cases have been reported. Meyer (Berl. klin. Woch., May 20, 1907).

**EPICANTHUS.**—This applies to the development of a broad fold of skin which extends from the inner border of the eyebrow to the side of the nose, its outer border being concave. This anomaly is usually associated with ptosis, or drooping of the upper lid over the globe.

### ACQUIRED ANOMALIES OF THE EYELIDS.

It sometimes happens after injury, and especially after burns, that the edges of the lids become united to each other. This condition is known as *ankyloblepharon*. If the adhesion occurs at the outer angle of the lids, *blepharophimosis* is said to be present.

**SYMBLEPHARON** is a union between the lid and the eyeball, and is generally the result of a burn or some severe inflammation of the conjunctiva which has produced great shrinkage of the conjunctiva and cicatricial change in the lids. The band of union may be but a delicate process of connective tissue, or the lid may be held down to the globe by an extensive cicatrix.

**Treatment.**—If the band be but slight, it may be severed by **ligature**; but if the attachment be more extensive, transplantation of healthy skin into the *cul-de-sac* may be necessary (**Teale's operation**), or the procedure of **Harlan** may be adopted. This author frees the lid from the globe by care-

ful dissection of the band of attachment, and then makes an incision through the whole thickness of the lid along the margin of the orbit. A thin flap is then obtained from the skin below the lid, which is turned upward, as on a hinge, so that its raw surface is brought into contact with the inner surface of the lid, while its smooth surface presents toward the globe.

The advantage of **paraffin plate** for holding mucous or Thiersch **grafts** in place in the fornix of the eyelids is obvious. It can do no harm to the cornea, and it can be built up as required to fit any conjunctiva *cul-de-sac* that has to be lined with a Thiersch graft. The graft will adhere to the paraffin, so that it can be evenly smoothed out on it, and thus perfect coaptation is secured between the graft and the raw surface of the *cul-de-sac*. To accomplish this, the graft should be thin and large enough to cover all raw surface, no suture being required. With perfect coaptation the graft will have secured a firm hold at the end of forty-eight hours and the plate can be removed for cleansing the eye. In case of restoration of the socket for prosthesis, it may be left in place for a considerable time, for the sac can be cleaned by irrigation through the holes in the plate. If it is so large that there is difficulty in removing it, it can be cut in two and the subsequent treatment continued with a plate that can be more easily inserted. The paraffin should be hard, with a melting point not lower than 150° F. (65.6° C.). The Thiersch graft should be thin and cut from the least hairy part of the arm or leg, and it is to be transferred to the paraffin plate directly from the razor. The plate is thus covered with the graft; the raw side outward is inserted into the new fornix. The author has thus operated upon 8 severe cases of symblepharon with good results. Wilder (Jour. Amer. Med. Assoc., Aug. 25, 1906).

Blepharophimosis may be corrected by dividing the outer canthus by a sharp pair of scissors, or by uniting the conjunctiva and the skin-surface by sutures.

**ECTROPION.**—Ectropion, eversion of the eyelid, may be caused by traumatism, especially burns, the cicatricial contractions drawing its tissues outwardly. Muscular or senile ectropion is seen in the aged, as a consequence of atrophy of the palpebral portion of the orbicularis and relaxation of the tissues.

**Treatment.**—In senile ectropion the deformity may usually be overcome by means of **Snellen's sutures**. This consists in burying a suture, which is entered at two points, one-third of an inch distant from each other, in the mucous surface of the lid, and passing deeply into the tissues between the skin and the mucous membrane. It is brought out upon the cheek, where the ends are tied over a piece of drainage-tube.

In cicatricial ectropion it is necessary to include in the **incision** the scar-tissue which has occasioned the eversion of the lid. If the cicatrix is small, **Wharton Jones's operation** will suffice. This consists in excising the cicatrix by means of a V-shaped incision. After the edges of the incision have been freely loosened from the sublying tissue they are approximated so as to form a Y. If the cicatrix be extensive, or if there has been much destruction of the skin of the lids and the neighboring tissues, **transplantation of skin** from neighboring or distant parts is necessary.

The writer recommends and describes a method which he has employed for many years with success in entropion and ectropion and some other conditions of the lids. It requires but two instruments which are

figured, a short **galvanocautery** point and a lid clamp. He usually employs local anesthesia with 4 per cent. cocaine on the conjunctival surface, but in nervous, sensitive patients it is necessary to employ nitrous oxide, bromide of ethyl, chloroform, or ether. If ether is used it must be removed before the approach of the hot cautery point. The lid clamp is adjusted with its straight bar 6 mm. from the lid margin. The galvanocautery point is applied to the surface with considerable pressure. The button on the handle is pressed down to turn on the current, while the point is quickly pushed through the cartilage and as quickly withdrawn. The punctures are made 4 mm. from the lid margin and separated from each other by an interval of 4 mm. These should be made on the side on which we wish the contraction to take place, namely, the conjunctival surface in ectropion and the skin surface in entropion. If necessary we can repeat in a few weeks. From one to three sittings will accomplish as much as would a plastic operation. He has seldom seen any reaction follow, but if there is a little cellulitis and puffing of the lid, the use of continuous ice-pads for a day or two will control it. Two or three repetitions are generally required, at intervals of from two to four weeks, according to the case. The procedure is perfectly under control. In repeating the operation it is well to alternate the punctures, locating the second series between the first. The eschar of the cautery causes no disturbance and usually clears off in about a week. Fourteen cases are briefly reported, showing the effects of the procedure in the class of cases for which it is adapted. S. L. Ziegler (Jour. Amer. Med. Assoc., July 17, 1909).

A new principle in the treatment of ectropion. It consists in **shortening the tarsus** at the temporal extremity and then attaching this extremity to the periosteum of the temporal border of the orbit on a level,

slightly above the lid commissure, if the lower lid is affected, and below the commissure if the upper lid is in fault. It is used for atonic ectropion, but the principle applies often also in cicatricial ectropion; 1 of these patients had undergone 6 operations without success. A. E. Davis (Jour. Amer. Med. Assoc., Nov. 18, 1911).

A detached graft of skin from the upper lid is recommended for the treatment of cicatricial ectropion of the lower lid of the same eye, or of the fellow upper lid. It is so removed as to cause no deformity of the upper lid, and when properly implanted will take and from the start match the corresponding tissues in color, texture, and pliability better than any other form of graft. J. M. Wheeler (Jour. Amer. Med. Assoc., Nov. 19, 1921).

**ENTROPION.**—Inversion of the eyelid, the margin, its lids being rolled inward, may be *spasmodic*,—i.e., due to overaction of the orbicularis through irritation from concomitant disorders, conjunctivitis, keratitis, etc., or to undue application of bandages after operation,—and *organic*, due to injuries, burns, ulcers.

**Treatment.**—The *spasmodic form* may readily be corrected by **excising a narrow strip of skin** from the lid parallel with its ciliary border. In *organic* entropion, on the other hand, it is necessary to **include the tarsus** in the operation, as this is usually distorted by the previous inflammation.

One of the best **procedures** for the cure of this deformity is that of **Hotz**. This is performed as follows: A transverse incision from canthus to canthus is made through skin and subjacent tissues, but, instead of being made near and parallel with the free border (as in the former methods), the incision is to follow the upper border of the tarsus. It therefore describes a slight curve begin-

ning and ending at a point about 2 mm. above the canthus, but being 6 to 8 mm. distant from the free border in the center of the lid. While an assistant is holding the edges of the wound well separated, the surgeon lifts up with forceps and excises with scissors a narrow bundle of the muscular fibers which run transversely along the upper border of the tarsus. The sutures, which are to include nothing but the cutaneous wound borders and the upper border of the tarsus, are then inserted. The first suture is placed in the center of the lid; the curved needle, armed with fine, black, aseptic silk, is passed through the lower wound border; there taken again in the needle-holder, it is boldly thrust through the upper border of the tarsus and returned through the tarso-orbital fascia just above this border, and finally it is carried through the upper wound border. One similar suture is placed at each side of the central one, and these three stitches are usually sufficient to draw the skin of the eyelid up toward the upper border of the tarsus and establish a firm union between these parts. This artificial union produces a slight tension of the tarsal skin, which, however, is sufficient to relieve any ordinary degree of entropion. But when the lids have been badly contracted—when the palpebral aperture has become unnaturally narrow or the free border of the lid has become entirely merged into the plane of the conjunctiva—these complicated cases require, in addition to the above operation, such surgical measures as **canthotomy**, the restoration of the free border either by **grooving the tarsus** or by **grafting**.

## **DISTICHIASIS AND TRICHIASIS.**

While distichiasis refers to the growth of the cilia along the outer marginal portion of the eyelid, trichiasis means a misplacement of the eyelashes. Both conditions are usually associated with entropion, especially when this condition is the result of chronic inflammation of the border of the lids.

**Treatment.**—**Epilation** or **removal of the cilia** by forceps may be tried if the stray cilia be not too numerous. **Electrolysis** may also be used in similar cases. Usually, however, **excision of the misplaced cilia** with the corresponding portion of the margin of the lid is necessary. This may be accomplished by making a V-shaped incision into the lid and by excising the flap so obtained, along with the truant cilia.

If the deformity be extensive, transplantation of the row of cilia is usually effected, and this is best accomplished by the **Jaesche-Arlt operation**. After a Knapp or a Snellen clamp has been applied to stop bleeding the lid is split in its whole length by a sharp knife; a second incision is then made through the skin of the lid about 5 mm. from its free margin and running its entire length. A semilunar flap of skin is then removed from the lid by carrying a third incision in a curve the entire length of the second incision. The edges of this incision are approximated by sutures, and the cilia drawn upward away from the globe.

WILLIAM CAMPBELL POSEY,  
Philadelphia.

**FORMIC ALDEHYDE**, or **Formaldehyde**.—This gaseous compound, discovered by von Hoffmann in 1867, is produced when a current of air charged with vapor of methyl alcohol (wood alcohol, or refined wood spirit) is directed upon an incandescent spiral of platinum wire, or spongy platinum. By means of a suitable condensing apparatus a liquid called *formol* may be obtained, which consists of a solution of formic aldehyde gas in methyl alcohol.

A watery solution of the gas is the *formalin* of commerce, which contains 40 per cent. of formaldehyde.

Formic aldehyde is also known as methyl aldehyde and oxymethylene.

When formic aldehyde is heated or strongly concentrated, it is converted into a white crystalline powder (*paraform*), which possesses most of the characteristics of formic aldehyde, owing to its gradual reversion to the gaseous state.

When *paraform* is volatilized it reverts to the gaseous form, but is redeposited as a sublimate in the crystalline form. Surgical dressings and bandages are impregnated with formic aldehyde in this way. The term "formaldehyde" is commonly used instead of the more correct term "formic aldehyde."

The writer confirms that the antibodies, except the antitoxins, are sensitive to formaldehyde, and in the same way as the Bordet-Wassermann substance. Forssman (C. r. de la Soc. de Biol., July 18, 1924).

A research to determine which bacteria tolerate formaldehyde best showed that, of the cultures of different strains of bacteria studied, colon bacilli and lactic acid bacilli displayed the greatest resistance to this very

active antiseptic, which is a normal product of their metabolism. L. Müller (C. r. de la Soc. de Biol., Apr. 11, 1924).

Experiments on mice showed that the toxicity of bacteria was at least 3 times weaker in dysentery vaccine treated with formaldehyde than when merely heated, while the immunizing power did not seem to be reduced at all. Experiments in the clinic confirmed in man this reduction in the toxicity by the formaldehyde, both for dysentery and for gonococcus vaccine.

Excellent results were obtained with the formaldehyde-treated gonococcus vaccine in acute gonorrhea. Durand (C. r. de la Soc. de Biol., Jan. 30, 1925).

**PREPARATIONS**.—When *formalin* (the 40 per cent. solution of formaldehyde gas) is heated in a dish or vessel, formaldehyde is disengaged and, at the same time, paraform crystals are deposited on the interior of the vessels. *Paraform*, or the polymerized form of formaldehyde, is also known as paraformaldehyde, paraformic aldehyde, triformol, trioxymethylene, and dry formalin, and occurs as a powder or in pastils. It is official as *Paraformaldehydum*, U. S. P.

*Liquor Formaldehydi*, U. S. P., is an aqueous solution of formaldehyde which contains 37 per cent. of the gas. It occurs as a clear liquid which is pungent and irritating to the mucous membranes. It mixes readily with water and alcohol in any proportion, but the solution becomes milky on standing owing to the separation of the formaldehyde from its excipient. It should be kept in the dark and in a cool place.

Various convenient preparations of these various agents are available in

the shops in the form of pastils, candles, etc., which greatly simplify their use.

#### PHYSIOLOGICAL ACTION.—

Formaldehyde has an intensely irritating effect on the mucous membrane of the eyes and air-passages. When injected subcutaneously in dogs, Pilliet observed congestion and degenerative change in the kidneys, liver, and spleen.

According to Benedicenti formaldehyde is a blood-poison. Introduced into the body, it causes excitement followed by slow asphyxia, and added to the blood outside the body it destroys the corpuscles and liberates hematin. The last body is formed without any preliminary change of oxyhemoglobin to reduced hemoglobin.

Formaldehyde appears in the urine in only 52 per cent. of patients taking urotropin. The reaction of the urine is of no importance. Alkalies, taken with or in combination with urotropin, have no effect on excretion. Urotropin is practically symptomless in an average dose. Patients not excreting formaldehyde are symptomless, regardless of the amount of urotropin taken. L'Espérance (Boston Med. and Surg. Jour., Oct. 24, 1912).

The writer gives the results of experiments made with *Burnam's test* for formaldehyde in the urine. His interest in the subject was aroused by the article of L'Espérance on the results of the reaction as tested in the Massachusetts Hospital. His own results are different in many respects from those of L'Espérance. Burnam's test consists in a color reaction in the urine of persons who have taken hexamethylenamine. The technique is given by L'Espérance as follows: "To about 10 c.c. of suspected urine in a test-tube at body temperature is added: (1) of solution phenylhydrazin and hydrochloric acid (0.5 per cent.), 3 drops; (2) of solution sodium nitroprusside (5 per

cent.), 3 drops; (3) of saturated solution sodium hydrate, a few drops poured along the side of the test-tube. As this latter solution diffuses throughout the urine in the tube, if formaldehyde is present (or the urine is positive), a deep purplish-black color is seen, quickly changing to dark green, gradually getting of a lighter shade of the same color, and finally pale yellow." When there is no formaldehyde in the urine a reddish color appears, changing to light yellow. The average time of appearance of the drug in the urine is about one hour after ingestion. It continues from four to six hours with its maximum at two hours. B. F. Jennes (Jour. Amer. Med. Assoc., March 1, 1913).

#### POISONING BY FORMIC ALDEHYDE.—

Concentrated aqueous solutions in contact with the skin act somewhat like carbolic acid. The skin becomes rough and whitish; a sharp stinging is felt if the skin is abraded.

Formaldehyde is a potent poison when the solution is strong or the quantity ingested large, differing but little in the degree of intoxication it produces from that of carbolic acid, *i.e.*, phenol.

Fatal cases have been recorded, in which the main symptoms were: A pricking or burning sensation in the pharynx and esophagus. Severe epigastric pain, which radiates in various directions, repeated vomiting of blood-stained mucus, vertigo, dyspnea, a weak and rapid pulse, unconsciousness — sometimes prolonged and suggesting cerebral apoplexy — lapsing into coma. The symptoms may come on at once if the poison is ingested while the stomach is empty; or they may be delayed, in so far as the general phenomena are concerned, if the

stomach contains food. A large dose may produce death in a few moments.

**Case of poisoning due to swallowing a quantity—about 1 ounce (30 c.c.)—of formalin.** There was vertigo, unconsciousness, and implication of the respiratory rather than the circulatory system. The predominance of cerebral symptoms, leading to early death, gave little opportunity for the development of signs of irritation of the kidneys and the alimentary canal, apart from the intense pain in the latter and the initial vomiting. Watt (*Brit. Med. Jour.*, Aug. 17, 1912).

The writer observed a case of a man of 42 who swallowed 300 Gm. (10 ounces) of a 40 per cent. solution of formaldehyde on an empty stomach. There was intense pain in the stomach, but no vomiting. The stomach was rinsed out an hour after the ingestion of the fluid. There was considerable vomiting after this, with almost pure blood in the vomit and stools, but then the condition improved for 4 days, when suddenly fever developed, with a violent cough and death in 6 hours. Necropsy confirmed that the spasm of the duodenum had kept the formaldehyde in the stomach; the intestines showed no signs of injury from it, and the changes in the kidneys were slight. The writer assumes that the elimination of the formaldehyde proceeded by the lungs, and the lung tissue was injured so severely by this that the acutely fatal toxic pneumonia terminated the clinical picture like an explosion as the formaldehyde accumulated in the lung tissue during the 3 days after the intake of the poison. There had been comparatively slight symptoms from the nervous system. Vercalli (*Policlinico*, Mar. 24, 1924).

Symptoms resembling anaphylactic shock were produced by the writer with injections of small amounts of formaldehyde. If it was mixed with serum and left for 24 hours the action was weaker. He explains it as direct irritation of the endothelial cells. No leukopenia nor lack of complement

was produced. Dold (*Klin. Woch.*, July 29, 1924).

**Treatment of Formaldehyde Poisoning.**—The most efficient agent to oppose the toxic action of formaldehyde is the official **solution of acetate of ammonium** (the spirit of Mindererus, with copious draughts of water. **Ammonia water** well diluted, the **aromatic spirit of ammonia**, or one of the salts of ammonium, especially the above mentioned, also in free dilution are antidotes. **Lavage** of the **stomach**, followed by the use of demulcents, **olive oil**, **starch water**, etc., are also beneficial measures. **Morphine** should be given hypodermically to relieve the suffering, which is usually very intense.

Large doses of **lime water**, a pint being given repeatedly, used in a marked case of formaldehyde poisoning. Shortly after taking the first dose the patient was able to speak and complained of very severe burning in his mouth and stomach. About fifteen minutes later the patient was able to walk. He did not get any other treatment, made a perfect recovery, and was perfectly sobered up. S. Fisher (*Medical Council*, July, 1904).

The writer observed 3 cases of poisoning. All recovered. The treatment consisted of a quart (liter) of **milk** by tube after the stomach lavage with diluted **aromatic spirits of ammonia**. **Milk of magnesia** and **strychnine** were also given. S. E. Earp (*N. Y. Med. Jour.*, Aug. 26, 1916).

#### USES IN DISINFECTION.—

The chief use of formaldehyde has been as a disinfectant. It permeates everywhere, is cheap and easily handled while less dangerous than corrosive sublimate. Its actual value after infections has been disputed, however, and it is now being somewhat less generally used than formerly.

In disinfecting a room the doors,

windows, etc., must be made perfectly tight, as the diffusive power of the gas is very high. The gas, which is very irritating to the eyes and respiratory tract, may be generated outside the room in one of the various generators to be had, and the gas conducted by a tube through the key-hole. Some forms of apparatuses are operated within the apartment. The pastils, candles, etc., available in the shops are thus used. After a sufficient amount of gas has been set free in the apartment, it is left for twenty-four hours. Length of exposure appears to be secondary to the quantity of gas used. An excess is recommended by most authorities.

Superficial instruments, bedpans, urinals, bedding, surgical dressings may be sterilized in small closets or in suitable receptacles. Formaldehyde does not seem to affect the coloring matter of the wall-paper, drapery, or garments (except light shades of violet and light red), and for this reason it is preferable to chlorine as a disinfectant.

Sodium dichromate used with sulphuric acid, gives results like those of potassium permanganate. Formula: Sodium dichromate, 10 oz. (300 Gm.); saturated solution formaldehyde gas, 1 pint (500 c.c.); sulphuric acid, commercial,  $1\frac{1}{2}$  fluidounces (45 c.c.). The acid and gas form a stable solution. After it cools it should be poured over the crystals of sodium dichromate, spread out in a vessel having 10 times the volume of the ingredients. The process is more rapid than with permanganate. S. G. Dixon (Jour. Amer. Med. Assoc., Sept. 19, 1914).

The writer recommends for disinfection of clothing commercial formaldehyde, poured into a saturated

solution of potassium permanganate. The mixture soon becomes hot and gives off abundant fumes which rapidly penetrate the clothing. The clothing may be placed in a large barrel, connected by a tube or pipe with a small barrel containing the mixture. F. Gand (Presse médicale, March 16, 1916).

If the fabrics or utensils can be moistened the action of the gas is rendered more active. A 1 per cent. solution suffices for all purposes. After the disinfection is completed the rooms should be aired for some hours, to rid it of all gas, owing to its irritating action on the throat and eyes. If the room must be promptly reoccupied, as in hospitals, hotels, barracks, etc., a 20 per cent. solution of ammonia sprayed into the room, by neutralizing the formaldehyde, rids the air of its pungency.

The procedure recommended by the Maine State Board of Health for the disinfection of rooms after their use by patients suffering from contagious disease is as follows: Potassium permanganate and formaldehyde are mixed together in the proportion of  $6\frac{1}{2}$  ounces of the former to each pint of the latter, and placed in a vessel of considerable size. The room is then closed for four hours, when disinfection is said to be complete. Two pints of the formaldehyde are to be allowed to every 1000 cubic feet of space. Both on the score of simplicity and cost the method has much to recommend it. (Treatment, Dec., 1905).

While urologists have used formaldehyde for the sterilization of sounds and cystoscopes, surgeons, obstetricians, and general practitioners have failed to avail themselves of its valuable properties. The experimental researches and clinical experience of the writer showed it to be in many respects superior to the methods of sterilization now in vogue. All porous materials



placed in a formaldehyde vapor absorb the latter until saturated. At room temperature this requires twenty-four hours, at the expiration of which the material exposed is completely sterile and remains so, showing that the micro-organisms have been not only inhibited but destroyed. Upon raising the temperature of the vapor to 45° or 50° C., sterilization is secured in half an hour; 55° C. should not be exceeded, as the formaldehyde then begins to decompose. The writers employ this agent for routine sterilization. The apparatus consists merely of metallic boxes, closing tightly, at a short distance from the bottom of which is a tray covered with powdered trioxymethylene; the latter, in turn, is protected with several layers of fine gauze, which prevent particles of the formaldehyde liberating powder from reaching the material to be disinfected when the box is heated. Surgical paraphernalia in daily use are sterilized with the warmed formaldehyde vapors, while other material is sterilized in the cold, being left in the box for forty-eight hours. Rubber gloves are in no wise injured by this procedure, as they are by boiling or steam under pressure. Instruments need not be boiled unless they have been used in septic operations. Suture materials not intended for resorption, and dressings, including protective silk, are easily sterilized without deterioration provided they are unrolled. Barthélemy performed 600 operations with all the materials used sterilized by formaldehyde, while F. Gross has done 1000 celiotomies and a like number of radical hernia operations with gloves thus treated.

The results, which were entirely satisfactory in these cases, lead the authors to recommend the method for widespread use, owing to its simplicity. Gross and Barthélemy (*N. Y. Med. Jour.*, from *Revue de chir.*, Jan., 1913).

Formaldehyde has the property of hardening nitrogenous substances of the nature of gelatin. This has been made use of in the preparation and sterilization of catgut. After this

method of preparation the catgut can be boiled without destroying it.

**THERAPEUTIC USES.**—**Gynecological Disorders.**—In **vaginitis** and **catarrhal endometritis** a tablespoonful of a 10 per cent. solution of formalin to a quart of water has been found useful. In **gonorrheal vaginitis**, good results have been claimed from the use of formaldehyde. The vulva was washed with a 1:1000 solution, and the vagina douched through a speculum with a strong solution, varying from 2:1000 to 5:1000. If the uterine cavity and cervical canal were involved, a weaker solution was injected. When there is laceration of the cervix, tampons soaked in 1:1000 of formaldehyde are left for two or three hours in the vagina. When fungous endometritis is present, the curette must be first applied. The applications give rise to no pain, and may be used daily, or every second day.

**General Surgery.**—Though a powerful antiseptic, formalin has been little utilized in surgery, owing to the intense pain and irritation it causes when applied to the living tissues. When, however, an excess of hydrogen peroxide solution is mixed with formalin, a chemical reaction takes place which destroys the formalin and completely checks its irritating and pain-giving properties.

J. Clark Stewart (*Surg., Gynec. and Obstet.*, Aug., 1911), taking advantage of this fact, applies the liquor formaldehyde, U. S. P., freely to infected wounds, leaves it in contact approximately one minute, and then neutralizes it by the use of hydrogen peroxide. It is important, he says, that an excess of hydrogen peroxide be used, in order that all formalde-

hyde shall be surely destroyed. If too little peroxide is used the chemical reaction is incomplete, and a certain amount of formic acid is produced, which is an irritant. From hospital and private experience with this mode of antiseptis, Stewart recommends it in the following clinical conditions:—

First, in **infected wounds**, it largely supersedes phenol followed by alcohol; it seems no more painful, and is decidedly more efficient. Wounds are thoroughly mopped out with the formalin, and after one minute or more if there is no pain an excess of peroxide is poured in, and the resulting foamy discharge wiped away. Often one such treatment will change an infected into a healthy wound, but in some the application must be repeated after one or two days. The coagulating and hardening action of the formaldehyde was not in evidence, owing probably to its neutralization.

Second, as a deodorant in **ulcerating carcinoma**. A 10 per cent. solution of formaldehyde applied by means of gauze on the ulcerating surface, the surrounding skin being protected by a thick covering of vaselin, will remove all odor and check discharges; but the author discovered that the pure formalin (officially 37 to 40 per cent. formaldehyde), controlled by hydrogen dioxide, answered the same purpose more quickly and with less pain.

Third, for the control of the fungus of **sarcoma**, with its troublesome hemorrhage and discharges. As soon as the fungus appears it is painted with formalin or cotton wet with formalin left in contact with it. If the skin is protected there is no

pain, and the fungus is soon changed into a black, leathery mass. After the subjacent pressure has increased, the sarcoma will burst through the hardened portion, and the process must be repeated. In some cases the hypodermic injection of formalin very superficially around the base of the fungus seemed to improve the condition. Care must be taken, both in injections and in applications, not to allow any surplus to invade the unprotected skin. In one case treated for fungus in the groin, the fumes alone seemed to irritate the scrotum; protection must be provided.

**Vesical and Urethral Disorders.**—Lamarque recommends the use of a 1 per cent. solution for irrigating the bladder and urethra and a 5 per cent. solution in **chronic gonorrhea**. In **hematuria and tuberculous cystitis** it has also proved of value.

Formaldehyde solution irrigations are especially valuable in **cystitis** associated with ammoniacal decomposition of the urine, such as occurs with enlarged prostate or tumor of the bladder. There are marked individual variations, however, in the tolerance of the vesical mucous membrane to formaldehyde, which are independent of the state of inflammation present. An acutely inflamed bladder is much more intolerant than a healthy one.

In **chronic cystitis** and in healthy bladders the writer found it practicable to use solutions varying in strength from 1:3750 to 1:7500. Occasionally a bladder was met with which did not tolerate even the latter solution, but no cases came under observation which would not tolerate a 1:12,500 solution.

It was found the kidney pelvis, injected by means of a renal catheter, would tolerate solutions as strong as the bladder. No irritation in the kidney itself was ever noted after such an irrigation. C. F. Burnam (*Arch. of Intern. Med.*, Oct., 1912)

*Ammonioformaldehyde* was found by E. L. Keyes, Jr., to be almost a specific in some cases of uncomplicated **acute catarrhal pyelitis**. To prove effective it may have to be administered in large doses until the urine is practically free from bacteria, after which a smaller dose may be sufficient. In judging the effects of the drug the centrifuge and the microscope should be employed. The dose must not be sufficient to cause pollakiuria and dysuria by irritation of the neck of the bladder. The possibility of such an irritation cannot be overlooked even when small doses are given.

**Cutaneous Disorders.** — Poitevin suggests the application of a layer of absorbent cotton dipped in a 2 per cent. formalin solution and covered with an oil-silk or rubber bandage in parasitic diseases (**ringworm**) of the skin. Its vapors diffuse readily, even through masses of fatty matter, which makes it specially suitable for the treatment of deeply implanted diseased hair, and also for the disinfection of the hair-follicles filled with sebaceous matter. In case of irritation of the skin, the bandage may be removed for a day. It has also been recommended in cases of **psoriasis** and **lupus** as a local application.

Formaldehyde in free solution is very efficient as a wash in **fetid sweating** and in **colliquative sweats**. A proprietary preparation termed "enformol," which contains formaldehyde and aromatics, is preferable to the plain solution in that it is not unpleasant to the patient.

Insects are readily killed by weak solutions of formaldehyde, and an easy way to get rid of flies (which are increasingly being associated

with infection) is to place 1 dram (4 Gm.) of the official liquor formaldehyde in a saucer of sweetened water, a solution which flies drink with avidity.

When a watery solution of gelatin is allowed to dry in formalin vapor the chemical characteristics of the gelatin are altered. It is no longer affected by hot or cold water, nor by acids or alkalies. Animal tissues, however, have the power of breaking up the combination and setting the formalin free. When the formalin-gelatin, ground to a fine powder and mixed with cultures of various forms of pathogenic bacteria, was introduced into animals, the bacteria did not develop, and the wounds healed without trouble. With this *formalin-gelatin powder* every **acute suppuration** can be stopped in twenty-four hours, and **wounds** made to heal aseptically.

Schleich has used it in **acute suppurative processes**, **aseptic wounds**, **compound fractures**, **deep scalp wounds** and other exposed lesions. The wounds were only cleansed mechanically, and then thoroughly rubbed with the powder. In cases of **necrotic masses**, in old **ulcers**, etc., the formalin-gelatin powder is dusted on the wound, and then covered with a dressing wet with the pepsin solution and the digestive process keeps up a continuous supply of formaldehyde vapor for the wound. The powder is made by drying 500 Gm. (16 ounces) of purified and dissolved gelatin in the vapor of 25 drops of formalin.

Schleich's formalin-gelatin was found of great value by Foote in the treatment of **suppuration**, giving the most perfect results in those cases

where the cellulitis is moderate and the pus abundant.

Good results from local application of formaldehyde are reported by R. L. Hammond (Amer. Med., July, 1912) in **verruca** (warts), **clavus**, (corns), **callositas**, **nevus pigmentosus**, and **cornu cutaneum**. Formaldehyde of 40 per cent. strength was invariably used, undiluted; a wooden toothpick or matchstick was dipped in it and the adherent drop applied to the surface of the lesion, every three or six hours for two or three days. Care was taken not to touch the normal skin with the agent. After several days, in the case of small excrescences, and in about a week, with the larger ones, an application having been made three times daily, it was found that pain was experienced, devitalization of the tissue occurred, and, upon discontinuance of the applications, the growths desiccated. After exfoliation the under surface or dermal layer appeared free from the blemish, or, if not, another application or two secured the desired result. If an open sore is produced, the author adds, a healing ointment of zinc oxide or simple cerate is usually all that is needed. In the case of small excrescences the applicator should be whittled to a fine point. In extensive callosities the remedy can be applied with a brush three times daily for several days, or until the surface becomes sensitive; then the applications should be stopped and the parts allowed to dry, when by soaking the epidermis with warm water it can be rubbed off. This process can be repeated until a cure is effected. In **cornu cutaneum** the horny growth should be clipped away as near to

the dermal attachment as possible and the agent then applied as often and thoroughly as it can be with comfort. Formaldehyde exerts a local anesthetic effect; but this does not protect against its own irritating action. Large and painful warts were, however, removed by its aid with much less pain than attends their removal by other agents, such as nitric acid, zinc sulphate, etc.

**Ophthalmic Disorders.**—Formaldehyde has been recommended as a disinfectant in **ulceration of the cornea**, the solution generally preferred for **collyria** being 1:2000. Stronger solutions should be applied immediately to the seat of the ulcer.

**Disorders of the Respiratory Tract.**—In the treatment of diseases of the nose, larynx, and lungs formaldehyde has been recommended by a number of observers, in solutions ranging from 2 to 40 per cent. Although these reports merit credence, the fact remains that the irritation produced is such as to deter many from using it in preference to other means.

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**FOURTH DISEASE.**—This is an infectious disease first described by Dr. Clement Dukes in 1900. It is thought to be to scarlet fever what rubella is to measles. According to Cheinisse, it is identical with *scarlatina variegata*. The cause of the disease is unknown.

It was not until the close of the seventeenth century that, mainly through the researches of Sydenham, scarlet fever ceased to be confounded with measles, and now, at the close of the nineteenth century, rose-rash is still confused with measles and with scarlet fever. Finally, on the verge of the twentieth century, it is being discovered that a fourth dis-

ease, perfectly distinct from measles, rose-rash, and scarlet fever, is to be distinguished. But whatever name for this disease should be ultimately adopted, it should preclude confusion with scarlet fever or rose-rash. Clement Dukes (*Lancet*, July 14, 1900).

In an encampment of the Italian army the writer observed 57 cases of this disease. Montefusco (*Riforma Medica*, Feb. 21, 1916).

The "fourth disease" (Filatow-Dukes) undoubtedly exists as a clinical entity. It should be differentiated from German measles by the scarlatiniform rash, and from scarlet fever especially by the absence of subsequent desquamation. The name "scarlatinella" is suggested. Hochsinger (*Wiener klin. Woch.*, Feb. 11, 1926).

**SYMPTOMS.**—The symptoms recall those of two diseases, viz., scarlet fever and German measles. The incubation period varies from about ten days to three weeks and prodromes are usually absent. The onset is usually abrupt, although malaise and sore throat are sometimes present. The rash appears suddenly, covering the body within a few hours. The face is oftentimes free from the rash. The latter is of a bright-red color and is followed by slight desquamation, although in some cases the desquamation is marked. There is usually a slight fever, the temperature rarely going above 101° F. and some glandular enlargement is present.

Summary of 19 cases of a series of this fourth disease: There were practically no premonitory symptoms and no illness was complained of until the rash appeared, but on inquiry admission of general malaise was elicited. In 1 case free vomiting occurred in the night and a very full rash was discovered in the morning. This vomiting arose, however from his having eaten freely of sweets in the evening. The maximum temperature throughout his illness was only 99.6° F.

The first symptom to attract the attention of the sufferer was the rash, which in nearly every case was very full and quite characteristic of scarlet

fever. The fauces were red and swollen, but occasioned so little discomfort that complaint was rarely made, and the condition was only discovered on inquiry or inspection. In some cases the skin became merely rough; in most instances there was free desquamation of small scales; while in others the peeling was equal to the worst ever noticed in scarlet fever. In this fourth disease the desquamation bears no relation to the intensity of the eruption; several of these cases with the fullest and intensest eruption were followed by very scanty desquamation. The peeling may continue as long as in scarlet fever, although it is apparently innocuous. The tongue was furred throughout, which cleaned as all furred tongues do. In no case did the tongue peel on the fourth day, as is so pathognomonic of scarlet fever in both mild and severe attacks.

The lymphatic glands universally were enlarged, hard, and tender, sometimes excessively tender. The average temperature was 101° F. (38.3° C.), but it ranged from 99.4° to 104.2° F. (37.4° to 40.1° C.). The temperature almost invariably became normal on the third or fourth day. In only 1 case did the pulse reach 100—a signal contrast to the accelerated pulse of scarlet fever.

In no instance did albuminuria arise, although all the sufferers except 2 were fed freely as soon as the slight fever (which occurred from the third to the fifth day) had disappeared, and the boys were removed from bed as soon as the rash had subsided.

It was impossible to ascertain the incubation period in this series of cases, since several of them occurred simultaneously. It is believed the incubation varies from nine days to twenty-one days. The duration of infectiveness lasts from ten to fourteen days or even twenty-one days, where efficient disinfection is in operation. The continuation of desquamation is apparently of no moment as a cause of infection or

**sequelæ.** Scarlet fever had not occurred previously in any instance. Eight boys had already suffered from rose-rash out of this series of 19 cases, or 42.1 per cent. Clement Dukes (Lancet, July 14, 1900).

The writer has been able to verify Duke's conclusions, and from his clinical experience noted that the disease usually lacked prodromal symptoms, with the exception of pain in the neck. In some of the more severe cases, however, there were noted for some hours headache, nausea, loss of appetite, pain in the back, and occasionally a chill. This agrees to rubella very well, but is in marked contrast to scarlet fever. The eruption is usually the first appreciable symptom which in the course of a few hours covers the whole body. This appears in the form of a small punctiform, thick beset, pale raw red, erythematous eruption that is not perceptible above the skin. It is also to be seen over the face, though here not so plainly. According to Dukes the lips and the dorsum of the nose are free. The pharynx is slightly swollen and injected. The cervical glands are hard and enlarged to the size of a pea. Occasionally the axillary glands and those of the groin are enlarged. The eruption is of short duration; the desquamation is fine and bran-like, lasting about fourteen days. Nephritis is seldom seen following the disease. The pulse is not rapid. The temperature ranges from 98° to 104° F. (36.7° to 40° C.), which is not increased during the eruption. On the fifth or sixth day the patient can usually be up and about. In fourteen to twenty-one days the danger of infection is passed. It seems as though various clinicians are divided in their opinions as to the condition being a disease entity or an abortive form of scarlet fever or rubella. Johnson and Bo Kay (Deut. med. Woch., Oct. 20, 1904).

**DIAGNOSIS.**—The disease must be differentiated from scarlet fever and

German measles, and may occur with either of these diseases. There are no sequelæ.

When one or more cases of apparent mild scarlet fever occur in a family giving a clear history of former attacks of scarlet fever, Dukes's disease may be suspected. Anomalous cases of doubtful diagnosis were exceedingly common during a recent epidemic of scarlet fever in Chicago, and many came to the writer's attention. There were but few cases of rubella, as we understand that disease. The health department reports represent less than one-fourth of the epidemic. Twenty-four physicians personally interviewed admitted having had 478 cases, though reporting only 117, the others being diagnosable only as suspicious. A. C. Cotton (Jour. Amer. Med. Assoc., Oct. 26, 1907).

**TREATMENT.**—The treatment is purely symptomatic. The diet should be light and nutritious. Rest in bed is essential, especially if there is much fever. During desquamation cleansing baths should be given and the skin anointed with olive oil or cacao butter. H.

**FRACTURES. —DEFINITION.**—A break in bone or cartilage, either partial or complete, is known as a "fracture."

**ETIOLOGY. —Predisposing Causes.**—*Age.*—Fractures are relatively less frequent in infancy and childhood, owing to the elasticity of the bones, and in old age, owing to the restricted activity of this period of life, while the greatest incidence occurs about the age of 30. Intra-uterine fractures rarely may occur from external violence, and multiple intrauterine fractures more often result from traumatism received during birth, especially from manipulations by the obstetrician.

*Sex.*—Fractures in middle life are ten times as frequent in men as in

women, and in general, fractures occur three times as frequently in men as in women, due to the greater vocational dangers. In infancy and between the ages of 50 and 70 the incidence of fractures in the sexes is about the same, but after 70 the incidence is greater in women.

*Season.*—Fractures are more common in the warm months, because of the greater exposure due to active outdoor work and sports. Fewer fractures occur in the winter season, although the incidence of fractures of the leg from falls upon the ice shows a proportionate increase.

*Location.*—In the order of frequency, the various bones are fractured as follows: Radius, humerus, ribs, femur, clavicle, fibula, metacarpus, tibia, skull, tarsus, phalanges, inferior maxilla, and patella; the hyoid, coccyx, and sternum are bones infrequently broken. Approximately 45 per cent. of the fractures involve the upper extremity, 35 per cent. the lower, 10 per cent. the trunk, and 5 per cent. the head (Scannell). The curved shafts and spongy ends of the long bones of the extremities serve to absorb violence and protect the body proper, although not infrequently they give way in doing so.

*Occupation.*—Hazardous pursuits and games predisposing those engaged to falls, blows, and the like, operative, *e.g.*, in riggers, football players, and heavy construction workers, favor the production of fractures.

Pathological changes in the bones predisposing to fractures are referred to under spontaneous or pathological fractures.

#### **PATHOLOGY.—Classification.**

—A. *According to Degree.*—1. Complete fractures, in which the bone is

divided in two or more fragments.

2. Incomplete fractures, in which the bone is not entirely divided. These include:

(a) "Green-stick" fractures, involving usually the radius, ulna or clavicle in persons under 15 years of age. The bone bends on the concave side and gives way on the convex side.

(b) Fissure, linear, or stellate fractures, in which there is a splitting or cracking, usually involving the flat bones of the skull and rarely the bones of the extremities except as a part of a complete or comminuted fracture.

(c) Depressed, "pond," or "gutter" fractures, chiefly involving the bones of the skull.

(d) Splinter fractures, apophysis fractures are those in which a small linear fragment or bony prominence is torn from the bone.

B. *According to the Line of Fracture.*—1. Transverse fracture, closely following the transverse axis, and usually found in the lower end of the radius, the femur, or in the short bones.

2. Longitudinal fractures, producing a split of a long bone—very rare.

3. Oblique fractures.

4. Spiral or torsion fractures:

(a) V-shaped.

(b) T-shaped.

(c) Y-shaped.

5. Comminuted fractures, in which the bone is broken in three or more fragments.

6. Impacted fractures, in which one fragment is driven into the other, producing fixation.

7. Compression or crushing fractures, occurring usually in the tarsal bones or spine.

8. Complicated fractures, in which there is associated an injury of an important adjacent structure, such as an artery, nerve, vein, joint, or viscus, or extensive comminution, or extensive destruction of soft tissues.

9. Subperiosteal fractures. In most fractures there is a laceration of the periosteum, although as a rule the periosteum is not completely divided. Rarely a fracture may occur with no tearing of the periosteum, and with little primary displacement. These fractures may be difficult to recognize without X-ray study.

C. *According to Location.*—Fractures are classified according to their location in the bone, *e.g.*, as fractures of the shaft, neck, condyle, tuberosity, or process, or an epiphyseal separation. Articular fractures are those relating to joints.

1. Intra-articular fractures are those lying entirely within the joint.

2. Periarticular fractures are those extending close to, but not into the joint. The terms intra- and extra-capsular are also used, especially in relation to fractures involving the neck of the femur.

3. Epiphyseal separation is common up to the age of 20, and in certain joints may occur to the age of 25. The separation may be favored by pyogenic, syphilitic, or tuberculous involvement of the epiphysis. The fracture runs through the diaphyseal side of the ossifying cartilage, and is usually associated with a laceration or stripping off of the periosteum. The most common locations are the upper and lower ends of the humerus, lower end of radius, lower end of femur, upper end of femur, and upper end of tibia. Recovery without deformity occurs, but

progressive deformity from interference with the growth of the bone is to be feared. If infected, the epiphysis may be destroyed and the joint invaded, with secondary arrest of growth and ankylosis, or more serious infection may necessitate excision of the joint or even amputation to save the patient's life.

D. *According to Application of Force.*—1. Direct, occurring at the point struck.

2. Indirect, occurring at a point distant from that where the force has been applied. These are divided, according to the form of force applied, into bending, torsion, compression, avulsion, and bursting fractures.

3. By muscular action.

E. *According to the Absence or Existence of Exterior Communication.*—

1. Simple fracture—a closed fracture, one in which there is no open wound in the skin—in contradistinction to:

2. Compound fracture—an open fracture, one in which there is an open wound in the skin communicating directly or indirectly with the line of fracture.

F. *Spontaneous or Pathological Fractures.*—These fractures may be classified according to cause as follows:

1. Agetic, as in osteoporosis, a congenital familial type of imperfect osteogenesis, with an inherited tendency to fracture.

2. Atrophic.

(a) Senile. In old age, central rarefaction with absorption of the trabeculae occurs, the absorbed bone being replaced by fat. The condition occurs prematurely in certain persons. Fracture from this cause most



frequently occurs in the neck of the femur.

(b) Dyscrasic, the atrophy of bone taking place from prolonged, debilitating disease such as typhoid fever or scurvy.

(c) Disuse. Prolonged immobilization or lack of use is followed by atrophy of the bone.

(d) Neurogenic. In tabes, syringomyelia, paresis, spina bifida, and after division of the peripheral nerves, atrophy of bone favoring fracture may occur.

(e) Pressure. An adjacent aneurysm or tumor, or other substance continuously pressing upon a bone, may lead to its absorption and final fracture.

**Pathologic Changes.**—(a) *Fragilitas ossium* occurs in children and disappears in adult life. Repeated or multiple fractures occur without impairment of the reparative function, so that the fragments usually promptly unite.

(b) *Osteomalacia* generally occurs in women, in association with pregnancy, the bones tending to soften and bend rather than suffer complete fracture. There is a marked deficiency in the mineral constituents of the bones.

(c) *Rickets* is associated with softening of bones, due to deficient mineral matter. The long bones, particularly the tibia, femur, and ribs, become bent and distorted. In scurvy-rickets, the epiphyses or the epiphyseal junctions are chiefly affected.

(d) *Inflammations of Bone.*—In pyogenic osteitis and osteomyelitis, during the period of separation of the sequestrum, a marked weakening of the bone favoring fracture may be

present. Central abscesses of bone occasionally result in fracture. The gummatous lesions of syphilis in the bone favor fracture. Fracture from syphilitic disease is much less common than from tuberculosis, and rarely involves the diaphysis.

(e) *Tumors of Bone.*—Sarcomas causing fracture are usually primary, and begin in the medulla. Reunion does not occur. Carcinoma of the bone is generally secondary, the primary growth being usually in the mammary gland, uterus, prostate, stomach, or other organ. The bodies of the vertebrae, the upper and lower ends of the femur, the upper end of the tibia, and the clavicle, are the localities most frequently involved. If immobilized, the fragments will at times unite.

(f) *Mycelomus and Neoplastic Bone Cysts, etc.*—Hydatid or echinococcus cysts of bone in rare cases lead to fracture. The diagnosis is made by X-ray examination, eosinophilia, the complement fixation test, or by surgical exploration.

**Bullet Wounds.**—A slowly moving bullet, one almost spent, if it strikes a bone will bore through it more or less completely and splinter it more or less widely in a manner that can be explained by the velocity, the angle of impact, and the quality of the bone; but with a swiftly moving, small-caliber bullet, another force has to be considered—that of vibration. If the vibration imparted to the bone by the projectile is such that the point of impact of the projectile coincides with a nodal point, the bullet will simply pierce the bone and no shattering will result. But if the point of impact does not coincide there will be more or less shattering at the point and at the extremities of the bone, the amount of shattering being dependent on the amount of vibration imparted to the bone. Now, the qualities in the bullet that tend to produce vibra-

tion are its momentum (weight and speed), which is imparted more or less to the bone as the bullet is larger or smaller and as its point is harder or softer. Consequently the shattering power of a bullet increases with its velocity, its weight, its size, and its capacity to flatten out when it strikes a hard object. Indeed, much depends on the energy transmitted to the tissues, and the energy of a missile is the resultant of the mass of the missile multiplied by the square of its velocity.

In bullet wounds of the cranial cavity, and to a less degree of the thoracic and pelvic cavities, the amount of damage is, again, often dependent on the vibrations produced, the waves set up by the passage of a solid object through a semifluid medium, more or less hermetically sealed within an unyielding envelope. Whereas the even passage of the bullet does comparatively little damage, the waves of motion it produces may suffice to literally blow the top of a man's head off.

**Repair of Fractures.**—A fracture is followed by the formation of a blood clot between and around the fractured ends, which is soon invaded by leukocytes and gradually replaced by fibroblasts and osteoblasts. On the second day there is a proliferation of the cells of the periosteum and bone marrow, and two days later the osteoplastic layer of the periosteum has been transformed into a vascular germinal tissue consisting of large polymorphous cells in a homogeneous or fibrillated matrix. Gradually the germinal tissue becomes differentiated, patches of osteoid and occasionally chondroid tissue appear, unite into trabeculae and later are transformed into bone. At the end of the second week the extremities of the fragments are covered by a multitude of young osteophytes and osteoid trabeculae which show the greatest proliferation close to the fracture about the periosteum (*periosteal callus*) and the endosteum (*myelogenic callus*). By the end of the second or the third week the gap is bridged by trabeculae, and between the bones the so-called *intermediary callus* is formed. The forms of callus are commonly termed:

(a) The sheathing, external, or ring callus; (b) the internal, central, or pin callus

and (c) the intermediary or definitive callus.

Callus formation is greatest about the diaphysis of long bones, less in the epiphyseal ends of small bones, in small cancellous bones, and in flat bones, such as the scapula and the bones of the skull. In the skull, usually no callus appears above the surface. In intraarticular fractures, the extracapsular callus is large, the intracapsular scant. A joint may be bridged by osteophytes, causing ankylosis. In incomplete fractures, callus formation is much more limited. Absolute immobilization, slight separation, and slight laceration of the periosteum are associated with slight callus formation. Complete and comminuted fractures, the extensive tearing of periosteum, splintering, and periosteal displacement favor excessive callus formation. Widely separated splinters may not re-unite, may be rarified or absorbed, become thickened, necrosed, or cause inflammation.

*Ossification* occurs in from 10 days, as for the small bones of the face, to 8 weeks in the case of the femur. In association with new bone production there is an active and progressive absorption of unnecessary bone by the osteoblasts. This progresses for months, contouring the rough edges, reducing the amount of extra callus, and at times reopening and restoring the medullary cavity.

If the vital energy of the bone-forming elements is not sufficient to form bony union, the callus remains fibrous. The usual causes of fibrous union are systemic debility, separation of the fragments, faulty immobilization, and the presence of foreign bodies—*c.g.*, wire sutures.

**Repair of Compound Fractures.**—If they heal by first intention their repair follows the same course as that of simple fractures, but when suppuration occurs partly detached fragments that would otherwise have lived are cast off, and the ends of the larger fragments also die, and act often for long periods of time as foreign bodies to which sinuses run, after all active suppuration has ceased. In such cases the dead bone should be cut down upon and removed. After suppuration none of the callus goes through a cartilaginous stage.

**SYMPTOMS.—Deformity.**—Under this head are included all the changes in appearance and dimension of the injured part. Some deformity is always present, dependent upon the contusion or laceration of the soft parts, or, what is much more important, the displacement of the bone-ends upon each other. Most of the various displacements can be recognized by the eye or finger, but if the seat of the suspected fracture is covered by a thick layer of soft tissues, and especially if the contusion of these soft parts has given rise to a considerable amount of superficial deformity, mensuration must be resorted to. Measurements are best taken from bony points at opposite ends of the bone whose fracture is suspected, and the shortening or lengthening ascertained by comparison with the distance between the corresponding points on the opposite side of the body (*e.g.*, the sound limb). Unfortunately, however, it is often impossible to take measurements with any degree of accuracy from two points on the same bone, consequently the rule that must always be borne in mind, *viz.*, for a comparison of the measurements of the sound and the injured limb these measurements must be taken with the limbs in not apparently, but really corresponding positions. Two other sources of error are: first, that the length of limb in some subjects is normally asymmetrical; and, second, that previous disease may have affected the length of some one of the bones measured. Circumferential mensuration of a limb is valueless, for the increase in circumference of the injured limb, in cases where the bone deformity can-

not be readily made out, is usually due more to the effusion of blood into the soft parts than the overlapping of the bone-ends. The deformity of the soft parts is such as is caused by whatever contusion or laceration they may have received. Generally speaking, the swelling increases for twenty-four to forty-eight hours, and then gradually subsides, its subsidence being hastened by treatment: a fact which is of the greatest importance in reference to the application of splints.

**Abnormal mobility** and crepitus are the two other objective symptoms of fracture and are pathognomonic. In exposed positions the former sign may be elicited by directly grasping the segments of the bone and moving either upon the other; in other cases (fracture of the surgical neck of the humerus) the surgeon must be satisfied with determining that the motions (rotation) of one fragment (the shaft) are not imparted to the other, as indicated by the immobility of one of its bony points (the greater tuberosity). Again, abnormal mobility near a joint may simulate abnormal mobility of the joint itself, and special care be necessary to differentiate between fracture and dislocation.

**Crepitus** is the grating sensation heard or felt when the two rough bone-ends rub against each other. The intervention of soft parts between the bone-ends, of course, prevents crepitus, which may, on the other hand, be simulated by crackling of coagulated blood, by roughened joint surfaces, by tenosynovitis, and by emphysema. Finally, be it especially noted that although abnormal mobility and crepitus are

pathognomonic, they are often by no means necessary to the diagnosis of fracture, and the manipulations which they require may be not only extremely painful, but also, by producing further lacerations of the soft parts, positively harmful to the patient.

**Loss of function** is usually present to a greater or less degree, and is due to the weakness of the part or to the pain evoked by motion or pressure; but this symptom is liable to be misleading, for, while one patient may use a fractured limb with great freedom, another may be totally disabled by a mere contusion. In the long bones and about joints the deformity is usually increased by active motion.

**Pain** is always present except in unconscious patients. It may be elicited by direct digital pressure over the line of fracture, in which case it gives a very fair idea of the location and the line of fracture, or it may be elicited by indirect pressure, *i.e.*, by crowding the two fractured ends together by pressure against the distal portion of the injured part. In the latter instance the patient will localize the point of greatest pain at the site of the fracture.

Pain may also be elicited by voluntary motion of the injured part against resistance, in which case the pull of the ligaments and muscles by a mechanism of "cross-strain" will cause the patient to localize the maximum point of pain in the region of the fracture.

The evidence thus obtained, together with a history of injury, is often sufficient evidence of a fracture. Certainly no case presenting

such pain so definitely localized to a given point should be treated otherwise than as a fracture.

**Auscultation and Percussion.**—

The percussion note over a fractured bone is changed by the interruption of vibrations. The interruption of the percussion sound waves may also be noted by percussing above the supposed seat of fracture while applying a stethoscope at a point on the bone below the fracture. Secondary suggillation and hemogenic blebs appearing four days to two weeks after the injury are suggestive of fracture. A black and blue discoloration back of the lobe of the ear, appearing after three days (*Battle's sign*), is strongly indicative of fracture involving the mastoid.

**Clinical Picture.**—Immediately after the accident the torn vessels pour out their blood into the tissues, and within a few hours edema sets in on account of the occlusion of the lacerated veins and lymphatics and the obstruction of others by the pressure of the extravasated blood. The temperature may rise a degree or two, blebs appear on the surface, and the tense skin becomes discolored by ecchymoses. The discoloration which may appear a few days later, as the blood extravasated among the deeper tissues makes its way to the surface, perhaps at some distance from the point of fracture, is a presumptive sign that a bone lesion exists. In from one to five days—more rapidly under appropriate treatment—the edema subsides and the swelling is reduced to a hard lump, the mobility of the fracture becomes less, crepitus is no longer obtainable as the fractured bone-ends become covered with granulations, and, finally, after a few

weeks abnormal mobility entirely disappears and the fracture is said to be united. But the patient is not yet well. Disease has stiffened the joints and weakened the muscles so that several weeks or months will be required before the limb regains its usefulness, while in cases where the proper care of the joints has been neglected they may remain permanently stiffened.

X-ray examination permits of diagnosis of fractures without displacement of fragments and in which the classical clinical signs cannot be obtained, *e.g.*, fractures of the carpal or tarsal bones, the tibial head, the posterior part of the internal malleolus, in fissure fractures of the skull, in incomplete fractures of long bones, and in sprain fractures. It permits of diagnosis in bones palpated only with difficulty, *e.g.*, the ribs under the scapula, the coracoid process, the pelvis and vertebræ, the radial head, and the neck of the femur. It simplifies the differential diagnosis between diaphyseal fractures and epiphyseal separation. Seth Hirsch (*Amer. Jour. of Surg.*, Mar., 1918).

**DIAGNOSIS.**—The diagnosis of fracture should always be made with the least possible manipulation. A consideration of the patient's history, together with careful inspection, gentle palpation, and accurate measuring will usually suffice. If not, gentle manipulation of the injured part may be made use of for the purpose of eliciting abnormal mobility or crepitus. To this end general anesthesia is of great assistance by relaxing muscular spasm and removing pain; but with these safeguards against further laceration thus removed, manipulation should be doubly gentle. Moreover, a slight, gentle movement will often be of

service when a brusque or violent one will fail.

**The X-ray.**—Since the advent of the X-ray sufficient data have been collected to show that an X-ray picture is not, in the large majority of cases, essential for the diagnosis of a fracture, but is an invaluable aid in determining the result of any given method of reduction and retention, and for the latter purpose should never be omitted. Certainly no delay in reduction should be permitted in order to obtain a radiograph.

In crushing injuries of the hand or foot, in fractures about the hip and shoulder, fractures of the pelvis, and in some injuries to the ankle-joint the X-ray is most serviceable in making a diagnosis, since the real bone lesion may be obscured by swelling or by the difficulty of finding any serviceable landmarks. In this type manipulation may only cause us to suspect a fracture, while the X-ray picture will, in the hands of experts, give a very clear idea of the bone lesion.

**Differential Diagnosis.**—**DISLOCATION.**—In dislocations there is restricted motion where there was motion before. In fractures there is motion where there was none before. Moreover, if, in dislocations the range of motion is increased in one direction, it is usually diminished in the opposite direction, while a fracture usually gives abnormal mobility in all directions. Crepitus is pathognomonic of fracture.

The writer defines a *fracture sprain* as an injury of a joint, the result of trauma, which involves the breaking of a small fragment of bone, and is associated with a stretching or tearing of the ligaments of the joint, or the forcible avulsion of a tendon

from its bony attachment. It is important to recognize a fracture sprain, because the prognosis and treatment are decidedly different from those appropriate in common sprain. Final results are usually perfect with proper treatment, but joint tuberculosis is liable to develop after this type of injury in susceptible patients.

The treatment consists in **adjusting and immobilizing** the joint for 4 to 8 weeks, according to the location and parts involved. **Massage** and **passive and active motion** should be instituted later than in ordinary sprain. A position which will relax muscles exerting unfavorable traction is necessary for perfect final results. Frequent locations of fracture sprain are the joints of the phalanges of the hand and foot, the styloid process of the ulna, the lower end of the radius, the head and neck of the radius, the tuberosities of the humerus, the trochanters of the femur, the tibial cartilages of the knee, the tips of the malleoli, and the os calcis. More unusual are the tearing away of deltoid or quadriceps attachments of the humerus and the tibia, respectively, the condyles of the humerus, the olecranon, the acetabulum of the ilium, the lower end of the tibia, and the astragalus. Sohmer (*Journal-Lancet*, Nov. 15, 1920).

In dislocation the head of the bone is in an abnormal position, *i.e.*, the bony relationships of the articular surfaces are disturbed.

**CONTUSION.**—Position and pressure for a few days ought to reduce the swelling of the soft parts sufficiently to permit a satisfactory examination. Contusions of the hip form the exception. If even the X-rays fail to clear up the diagnosis satisfactorily, the only safe treatment is that for fracture.

**PROGNOSIS.**—The prognosis depends on many conditions, the extent of the injury, the associated

lesions, and the age and general condition of the patient. Again, the prognosis for certain fractures (clavicle, Colles's) is far better than for others. Among the accidents that may imperil the patient's life are *embolism* of a clot from an injured vein into the heart or lung, causing instant death (see EMBOLISM), or *fat-embolism*, a very rare condition which occurs during the first few days after fracture. The symptoms may be those of embolism or shock, or there may be more or less characteristic signs of edema of the lungs. Post-mortem examination reveals the fact that the pulmonary capillaries are obstructed by minute globules of fat, which have been poured into the gaping vessels from the torn bone-marrow. If the patient recovers, the diagnosis of fat-embolism cannot be made with any certainty.

Shock is a frequent cause of death, which usually occurs within the first forty-eight hours, and in compound fractures death may occur from hemorrhage, or later from tetanus or septicemia or pyemia. Delirium tremens is a frequent complication. The shock, the withdrawal of customary alcoholic stimulation, and the confinement to bed all tend to induce it. Besides the customary administration of hypnotics, stimulants, and nourishment, it is of the greatest importance to get such patients up and about while they are still in the premonitory stage of restlessness and insomnia. They must be gotten out of bed at any cost. I have seen this expedient succeed in abating an attack of delirium tremens when all other means bade fair to fail. Finally, gangrene may result from laceration of the main vessels of a limb

or from their compression, whether by the displaced fragments or by a splint unskillfully applied.

Local sloughing of the tissues may occur from the pressure of a sharp point of bone, or, more commonly, by extravasated blood. The reduction of the fracture, followed by the application of heat and pressure and the elevation of the limb, constitute the elements of prophylaxis in such cases, to which must be rarely added incisions for the evacuation of clots or the ligation of bleeding points.

Other early complications are the secondary compounding of the fracture by a sharp point of bone, and the formation of a traumatic aneurism in a lacerated artery.

Complete recovery may be delayed or prevented by exuberant, painful, or weak callus. The callus always is "exuberant" at first, and may be expected to grow somewhat smaller even after bony union has taken place, but experience has proved that large masses of callus that impair function will not disappear in the course of nature nor under any medical, mechanical, or electrical treatment. They must be exposed and chiseled away, and in this connection it is well to remark that in old cases it may be impossible to tell before operation whether the offending mass is a badly reduced fragment or exuberant callus. Persistent pain in the callus may be due to pressure on a nerve or the inclusion of nerve-filaments in the callus, or to supuration about a sequestrum.

Weakness of the callus, when it is not caused by undue separation of the fragments or constitutional debility, is usually due to inefficient immobilization. It is not an uncom-

mon consequence of supuration in a compound fracture.

Stiffness of the joints is, to a certain extent, the natural result of the immobilization necessary to secure union in the fracture. But this stiffness should be transitory except in the old and rheumatic, or unless the joints are sprained or involved in the fracture. In this last event permanent bony union of the apposed bone-surfaces may occur, or exuberant callus may interfere with the movements of the joints. The joints of the fingers, however, are very liable to remain stiff if they are immobilized for more than two weeks, especially if in the position of extension.

Atrophy of the muscles may be permanent in old and debilitated persons. In whom also spontaneous dislocations and fragility of the bones may result from disease.

Tumors—primary sarcoma and secondary carcinoma—may occur at the seat of fracture, and secondary carcinoma may occur in the epithelium lining of the old sinuses of compound fractures.

Permanent paralysis may result from laceration of or pressure on the nerves.

**TREATMENT.**—The treatment of any given fracture must vary with the type of the fracture, but in all cases the result to be desired is a restoration of function as near that of the normal function as is possible under the existing conditions.

The first essential in the treatment of all fractures is rest of the fractured area, and this rest should be secured at once on the spot at the time of the injury by some handy form of fixation to allow for the transportation of the patient to a

place suitable for carrying out the detail of fracture treatment. Binding the arm to the body, bandaging the two legs together, the use of branches of trees, pieces of wood, etc., may be mentioned for this purpose. Hasty attempts at reduction under unfavorable conditions result in failure to bring about proper reduction, and cause the patient unnecessary pain, and may also cause a simple fracture to become compound. In war surgery, fixation upon the field of battle before transportation has been found of the utmost value, preventing shock, pain, and complications from the shifting and movement of the fractured bone ends.

When confinement to bed is necessary the bed should be narrow (a single iron bed), the mattress firm and any sagging of the mattress due to the weight of the patient should be prevented by placing a board or boards which should rest upon the sides of the bed, *beneath* the mattress.

With the patient under favorable conditions the next step in the treatment, unless associated injuries or shock demand instant attention, is the reduction or setting of the fracture. Excessive subfascial swelling and impaction without development are contraindications to immediate reduction. Obviously many fractures, such as fractures of the ribs, require nothing but immobilization. Reduction may be done by manipulation, by open operation, or by various types of traction apparatus, and a judicious selection of the method of reduction is a primary essential for a favorable result.

If reduction of the fracture is im-

possible after the use of morphine hypodermically, a general anesthetic should be used. The nature of that anesthetic must of necessity vary. Nitrous oxide and oxygen, ether, and chloroform must be chosen or rejected for the same reasons as exist in the general field of surgery. In children a satisfactory reduction cannot be obtained without an anesthetic.

Certain types of fracture are particularly suitable for immediate reduction by manipulation, of which one may mention Colles's fracture, Pott's fracture, fractures of both bones of the forearm and leg, fractures of the clavicle, etc. Careful palpation will readily determine the position of the fragments and, by using the more superficial bone as a guide, one may determine fairly accurately the degree of reduction obtained.

Reduction by traction may be used, as (1) Traction by weight or weight and pulley (see Buck's extension). (2) Traction by suspension (Hodgen's splint or vertical suspension—Balkan frame, etc.). (3) Traction upon specially made nails driven into the lower fragment and to which the extension weight is fastened (Steinmann pin or nail, ice-tongs, or stirrup on os calcis).

The author's method consists in using a metal **extension apparatus** applied at once, after which the patient is allowed to get up and walk. Extension is maintained by a hollow metal rod into which a solid one glides, with a spiral spring. By driving pegs into suitable holes the apparatus can be made rigid at any desired length. The points of support are metal or plaster rings passed around the upper and lower ends of the fractured bone, leaving the joints free. Delbet (Rev. de chir., xxxiv, 249, 1915).



Give **morphine** for severe pain. Reduce the fracture as soon as possible, within 2 hours from the injury, under an anesthetic. Have an X-ray taken before reduction, if possible, without delaying it beyond 2 hours, and always have the plates made promptly after reduction. In all fractures treated by traction the plates should be made with the traction apparatus applied and in full operation. If the fracture is plainly irreducible or if not properly reduced, other treatment should be instituted as soon as possible. J. M. Hitzrot (N. Y. State Jour. of Med., July, 1917).

The principle upon which the newer methods of fracture treatment are based is that when the proximal fragment is at physiological rest, this is the position in which antagonistic muscles have brought it, and it will not have much tendency to move in either direction. If the upper fragment is in that position, the other fragment can be readily moved. Having placed the upper fragment in the position of physiological rest the distal fragment is brought into line with it, and then the whole extremity can be moved without moving the fracture. The use of the **overhead suspension frame** in high fractures of the humerus gives uniformly good results. After a time the arm is left free during the day and put back in suspension at night, and in this way union is often obtained in 18 or 20 days. J. A. Blake (Med. Rec., Apr. 3, 1920).

Since the World War, surgeons have been using **suspension** with the **Balkan frame**. When steady traction is necessary to retain the fracture during the application of the splint, the Hawley table is good. With suspension the Balkan frame is of value, but requires skill in adjustment. In **Buck's extension** too little weight is usually employed. **Massage** may be begun as soon as spasms have ceased, and should be repeated every few days, as it shortens convalescence. W. L. Estes (Med. Rec., Sept. 4, 1920).

The writer refers to the tendency to redisplacement which exists in the drying of plaster casts as ordinarily applied. To secure better results, he advocates a **3-plaster method**. The joints above and below the fracture are first encased, and the plaster allowed to set. Reduction of the fracture by manipulation or traction is next effected, and the middle section then plastered. Royle (Med. Jour. of Austral., Aug. 9, 1924).

The writer lauds **direct leverage** for the reduction of fractures after a reasonable effort at manual manipulation has failed. The type of lever used is a dental probe with rounded end or, if a heavier lever is needed, a  $\frac{1}{4}$ -inch round steel rod 8 to 12 inches long. For insertion of the lever a small stab is made with a scalpel at the most suitable point for leverage, and the lever then passed between the ends of the fragments. Reduction having been obtained, a **cast** is applied, anchoring the lever in the position which maintains the fragments. Where fluoroscopy is unavailable, traction is first made, and then a small incision for insertion of the lever and the index finger to the bone fragments. J. E. M. Thomson (Surg., Gyn. and Obst., Sept., 1924).

For the best results, traction should be made in the axis of the proximal fragment when it is in a position of relaxation.

For traction, bandages of fabrics may be fixed to the skin by various glues. The Venice turpentine glue or mastic is especially valuable. The Heusner and Sinclair glues require heating. Glue adhesion is effective for two to four weeks, and produces skin lesions much more rarely than does adhesive plaster.

*Heusner's glue:*

<i>Resin</i> .....	50
<i>Alcohol</i> .....	50
<i>Benzine (pure)</i> .....	25
<i>Venice turpentine</i> .....	5

This is removable with benzine or alcohol.

*Sinclair's glue* (modified) :

<i>Isinglass</i> .....	50
<i>Glue</i> .....	50
<i>Water</i> .....	50
<i>Calcium chloride</i> .....	2
<i>Tannic acid</i> .....	12
<i>Thymol</i> .....	1
<i>Glycerin</i> .....	2

For use, melt in water bath and apply with palm of hand or brush, without shaving the part. It may be removed with water.

A limb to which adhesive plaster is to be applied for purposes of traction should be shaved, wiped with alcohol, and the adhesive plaster applied. Traction should then be made with a sufficient degree of abduction and flexion to bring the limb into proper alignment and maintained by a weight sufficiently heavy for that particular case. The more rapidly extension is produced the better; therefore heavy weights should be used early.

Where traction bands cannot be applied to the leg, the Steinmann pin, which passes under the tendon of Achilles and bears on the os calcis, or tongs applied to the condyles of the femur, may be used.

The result of such traction should be controlled by daily measurement, palpation, adjustment of the alignment, and by an X-ray picture with the traction apparatus and its accessories in action during the radiographing of the fractured area.

If the above procedures show measurements and alignment practically identical on both sides too much stress must not be placed upon minor degrees of displacement as shown by the X-ray. Should the traction not bring about reposition in a week or ten days, it should be discarded.

[The Board of Medical Officers of the A. E. F. suggested that with three types of

wiring, traction and counter pressure fixation splints embodying the Thomas principle, the Jones cock-up "crab" wrist splint, the long interrupted Liston splint with adjustable foot piece and anterior thigh and leg splint (Hodges type), the Cabot posterior wire splint, the wire ladder splint material with light splint wood and plaster-of-Paris bandages, and Bradford frames, the treatment of all bone and joint battle casualties could be efficiently carried out at the front and in base hospitals. On practical application, 7 of these splints were found to fill nearly every need. The results obtained in fractures of war compared more than favorably with those previously obtained in civil practice.—W. WAYNE BABCOCK.]

**Operative Treatment.**—Open operation is indicated in fractures of the patella and the olecranon with separation of the fragments, in fractures which cannot properly be reduced by other methods, and in articular fractures when the displacement if uncorrected may seriously interfere with the motion of the joint.

The operative treatment of fractures is more strongly indicated in fractures in persons over 15 years of age. Below 15 years, good results are obtained by non-operative methods in most fractures, except those involving both bones of the forearm.

Primary operations for fracture give much better results than delayed or secondary operations, and in good hands the mortality is so small that it is not an argument against open treatment. The eighth day after the injury is the best time for treating closed fractures by operation. At this time the tissues have largely recovered from the primary traumatism and are in condition to withstand the added insult of the operation, while after the tenth day

the parts are set in callus and granulation tissue, and the operation more seriously interferes with the reparative process. Open operations aim at the exact replacement of fragments, reduction being maintained by various devices such as follow:

A. *Wiring*.—Aluminum bronze wire, on account of its strength and resistance to corrosion, is preferred. Annealed steel wire may be used where aluminum bronze wire is not available, for although it oxidizes in the tissues it has strength which silver wire lacks.

B. *Nailing*.—Nails of homologous or heterologous living or boiled bone, ivory, bronze, steel, magnesium, silver or other metal, may be used. Nailing is chiefly employed to hold separated fragments about the joints, as in fractures of the condyles of the humerus and of tuberosities. Nailing is at times valuable in fixing the lower fragment of the fibula in Pott's fracture and in holding the fragments in fracture of the neck of the femur. Instead of nails, screws or bolts may be inserted in holes previously drilled to receive them.

C. *Plates*.—The bone fragments may be fastened together by plates of metal, ivory, or dead or living bone. Metal, bone, or ivory pegs, nails, or screws may be used to fasten the plates in position, and the plates may be inlaid or dovetailed in the fragments. The preferred material is living bone taken from the same patient. Dead bone, ivory and metal plates are well tolerated by the tissues, in the order given. Steel plates frequently have to be removed by secondary operation, and may delay union or produce local irritation. They have the advantage of avail-

ability and ease of application, but during the last few years have been largely discarded. Magnesium plates, suggested by Payr, while absorbable, produce adjacent tissue reaction and may be expelled, and are not, as a rule, to be advised. Bolts with threaded nuts, made of metal, or better, ivory or bone, are at times of value.

Adjustable external plates fastened to the fragments by screws or bolts have been advised by Parkhill, Keatley, Freeman and Lambotte, but necessitate external communication with the area of fracture, favoring infection, and are of limited strength and soon become loosened, permitting displacement; in general, they have little to commend them.

D. *Bands*.—The band of Parham-Martin is made of annealed steel, and is passed around the fracture, the tongue end being passed through a slot at the other end, the band tightened and clamped about the fracture by a special instrument, and the surplus metal cut away.

E. *Sliding Bone Inlays*.—Bone inlays from one of the fragments, or transplants taken from the tibia, as advised by Albee, produce the least irritation and best fulfill physiologic indications. Bone transplants should not be devitalized in their removal, and should have living periosteum and endosteum attached. They are fixed in position by sutures of kangaroo tendon or catgut, or by bone pegs or nails.

F. *Strips of periosteum* with attached scales of bone may be stretched across the gap or wound around the fracture (Codivilla).

No fixation is necessary when the two fragments can be held in align-

ment without it. Only strong catgut or kangaroo tendon is necessary in cases with slight tendency to displacement.

In using **inlay grafts** as a substitute for Lane plates in ununited and fresh fractures (especially comminuted fractures), the author uses a universal motor, with a small saw for deep cavities, such as laminectomies, his twin saw, and a device by which the distance between the saws can be adjusted. This outfit is not absolutely necessary. In favorable subjects the entire graft may retain its viability, the inlay method bringing together each of the 4 layers: periosteum, compact bone, endosteum, and marrow. The bone graft is still more efficacious in gun-shot or other fractures where there is comminution or sequestration. In fresh fractures of large bones, to prevent the inlay from slipping into the marrow cavity, the graft and gutter beds are made wider at the periphery. With the fragments in proper alignment, the graft is usually removed from the fractured bone, generally the proximal fragment, and then slid distally into a groove one-half its length prepared for it in the distal fragment. In the femur the sliding inlay is made 5 or 6 inches long. In long bones with difficulty of fixation, the inlay is held by bone graft pegs or heavy kangaroo tendon, or both. Albee (*Med. Rec.*, Mar. 20, 1915).

Where there is deformity or overriding, the writer puts in an Albee **sliding graft**, or puts the ends in position with clamps, and then fastens them, 2 holes being drilled through each fragment in such direction that, when **kangaroo tendons** are passed through, they cross each other in the medullary canal and hold the ends in apposition without slipping. In overlapping or oblique fractures, the holes are drilled straight through, the gut being passed in and out and tied as a mattress suture. Two of these are sufficient. Lathrop (*Annals of Surg.*, July, 1916).

Oblique fractures do well on some form of **encircling wire** or **band**. The best is that of Parham and Martin. By using 2 bands, spiral fractures with comminution may be treated. In children the bone grows over the band, and includes it. Lund (*Surg., Gynec. and Obstet.*, Nov., 1916).

The use of the autogenous bone graft requires great mechanical skill, making its routine use impossible except for the specially talented. Its use for the average surgeon is restricted to ununited fractures where there is little tendency to displacement. Use of the **Parham band** in oblique fractures is recommended since it is easily applied with the "no hand touch" technique, introduces a minimum of foreign material, and holds the fragments firmly in position. The **intramedullary graft** for transverse fractures is also easy and effective. For fractures of the neck of the femur or humerus the **bone peg** is useful but can often be satisfactorily supplanted by the use of a long **wire nail** or **skewer** to be later removed. Perfect anatomical reposition, especially about joints, is not necessarily followed by a good functional result. E. Fischel (*Jour. Mo. State Med. Assoc.*, xv, 291, 1918).

Describing the use of **intramedullary beef-bone splints** in fractures of long bones, the writer states that such splints are easy to apply and afford great strength. In applying a long intramedullary splint, beef tibia or femur about 5 or 6 inches long is made into strips  $\frac{3}{4}$  inch in diameter for the adult femur and  $\frac{5}{8}$  inch in diameter for the humerus. A hole is bored near one end like a needle eye. The splint is driven into the medulla of the long fragment, eyeless end first, and the eye threaded with catgut. A hole is then drilled obliquely through the cortex into the medulla of the short fragment. This hole slants toward the break and is placed at a distance of one-half the splint-length from the fracture. Through it wire is threaded, brought out at the end, and fastened to the catgut which has been

previously attached to the hole in the splint. The fracture is then reduced and by means of traction on the wire and catgut the splint is drawn into position. To keep the splint from slipping the catgut may be sewed to the periosteum. E. W. Ryerson (Jour. Amer. Med. Assoc., lxxiii, 1348, 1919).

The writer considers the **autogenous one graft** far superior to plates and screws in open operations for simple fractures. Stress is laid on the importance of asepsis. It is recommended that 2 or 3 inoculations of *Staphylococcus aureus* vaccine be given prior to the operation. B. Hughes (Lancet, cxcviii, 595, 1920).

The writer uses **ox bone plates** in his fracture work. The plates are made in various sizes, the length, width and thickness being adjusted to the requirements of stress for the particular fracture in question. W. Cunningham (Wis. Med. Jour., Oct., 1924).

**Splints.**—Retention after reduction is usually maintained by some form of splint. For all practical purposes only three types of splints need consideration, namely, wooden splints, molded plaster splints, and circular plaster encasement.

*Wooden splints* should be long enough to include the proximal and distal joints, wide enough to prevent compression of the limb, and sufficiently padded to prevent pressure upon the skin, especially over bony points.

*Molded plaster splints* (introduced by Stimson) conform most readily to the demand for proper fixation, strength, lightness, ease of inspection and removal. They are made by measuring the desired length with a piece of bandage (Canton flannel). Upon this the ordinary roller plaster bandage is carried back and forth, carefully smoothing each layer of the

bandage as it is laid until the desired thickness is obtained (care should be taken not to make the splint too thick). While still plastic the splint should be molded to the limb and bandaged into place, avoiding circular turns of the retaining bandage. The splint rapidly hardens and, if properly made and applied, will maintain the most efficient fixation. All that is necessary for inspection of the fracture is the removal of the bandage, for, when hard, the splint readily keeps its position—with very little assistance during the process of inspection.

*Circular plaster encasement* is still the favorite method with many. Its application must be made smoothly without compression and all bony projections well padded along the sides so that pressure will not come upon the skin over the bone. The toes and fingers must always remain exposed. After its application the fingers and especially the toes must be carefully watched and, if they become cold or blue, and the patient complains of pain, the cast must immediately be removed. Gangrene of the leg may result if the above is not done.

If circular plaster is used many writers advise cutting down the front of the cast while it is still wet and before the plaster has hardened. When the plaster has become firm the cast is held closed by an ordinary roller bandage wound about it.

*Adhesive plaster* is used in certain fractures for purposes of fixation (*vide* FRACTURE OF RIBS, CLAVICLE, etc.).

**After-treatment.**—**Massage** should consist of gentle centripetal stroking, and whenever possible without removal of splints, should be instituted

beginning the second day. Where the splints are removed, it should be begun at the end of the second week in fractures of long bones, and at the end of the third week in fractures of the femur. Such passive movements of adjacent joints as may be carried out without disturbing the splints should be started on the third day.

In fractures involving the joints passive motion should be used, carefully bearing in mind the fact that such motion should be well within the limits of pain. It should never be forced. Forcible movement under an anesthetic should never be done. In general, the earlier **active and passive motion** is allowed, within the limits of pain, the better the result. Obviously no weight should be borne by a bone or bones which are not yet solid, without additional external support.

**Baking with dry heat** (160° to 300° F.) for one-half hour daily is a great aid in treating the joints. **Electricity** for the preservation of muscle and bone activity should be used more frequently than at present. Both the baking and electrical treatment may be begun at the end of the second week.

In the treatment of fractures, it is important to prevent secondary complications, including bed sores, pressure sores, interference with the circulation from tight splints or bandages that may lead to muscular degeneration and Volkmann's contraction, and the production of static deformities such as drop toe.

The writer pleads for the use of **electricity** in the treatment of fractures, basing his opinion on the results obtained in 758 cases. He makes

daily applications of the anodal galvanic current as a part of the treatment. Benefit results (a) with very weak anodal currents, (b) with a distant cathode, (c) with a wide surface of even entry, such as provided by water, (d) with the positive pole more than covering the whole of any muscles involved in the original injury. The anodal current is definitely the more sedative and soothing. **Diathermy** is, up to a certain point, as successful as the direct current. Heald (Brit. Med. Jour., Apr. 26, 1924).

**Compound Fractures.**—If the wound leading to the fracture is small, clean, and not contused, as is usually the case in compound fracture by indirect violence, the wound and any projecting ends of bone should be thoroughly cleansed, the skin painted with tincture of **iodine**, the fracture reduced with as little enlargement of the external wound as possible, the wound loosely sutured, and primary union expected. In case the wound heals aseptically the course is that of a simple fracture, but, if suppuration sets in, the wound must be promptly opened up, thorough drainage provided for at dependent points, after which the healing is concluded under local treatment appropriate to granulating wounds.

If, on the other hand, suppuration has already set in or seems inevitable from the contusion or the dirty condition of the tissues, provision must be made at once for thorough drainage. The skin should be painted with tincture of **iodine** and the lacerated wound filled with **balsam of Peru** or an **iodine-guaiacol solution** (iodine, 1; potassium iodide, 2; guaiacol, 5; glycerin, 100).

The latter is preferred. After such treatment a bulky dressing should be applied and the part put at rest. The

guide to the investigation of such a wound is the temperature. If the temperature remains low (101° F. or lower) the wound had better be left untouched for from five to seven days. Of course, in the presence of evidences of existing suppuration, the surgeon may not hesitate to institute the most vigorous antiseptic treatment, but in doubtful cases the disturbance incident to frequent changes of dressing will certainly result in suppuration, while the expectant treatment may have a happier issue.

The necessity of removing detached fragments of bone depends almost entirely upon the prospect of suppuration. In a clean wound fragments that are entirely detached may live, while in the presence of pus even the ends of large fragments will be cast off.

To estimate the amount of sloughing that will occur Es-march's artificial ischemia is a safe guide, those parts being doomed to which the blood does not flow on the removal of the bandage. But it is inadvisable to attempt any extensive clearing away of dead tissue until the bone has begun to granulate and the line of demarcation has formed.

In case of doubt it is always safe to delay amputation until it is clearly impossible to save the limb. Thus the patient is given every chance and the surgeon may avoid being sued for malpractice.

As to suppurating compound fractures of the larger bones, they need almost never be despaired of, from twelve to eighteen months being none too long for their ultimate and satisfactory recovery.

The treatment of compound and

gunshot fractures developed as a result of experience in the world war is as follows:

*A. Pre-inflammatory Period.—Primary or delayed primary closure.*

1. With a small opening and but little tissue destruction, the area of the wound should be sterilized, devitalized and dirt-impregnated tissues débrided with a very sharp knife, the marrow cavity curetted to a depth of 2 or 3 centimeters, splinters, foreign bodies and necrotic and econotomic marrow removed, careful hemostasis carried out, the fracture reduced, and the part immobilized and carefully watched. If evidence of infection develops, the wound should be freely opened, detached bone fragments and foreign bodies removed, and the wound drained with a copious wet dressing or by the Carrel-Dakin method. Delayed primary closure should be deferred until the fourth day and should not be attempted when streptococci, staphylococci, or large bacilli are found in the wound excretions. Isolated cocci or diplococci do not prevent closure.

2. Cases of extensive local destruction of tissue, with or without the presence of foreign bodies in the wound, should be treated by immediately sterilizing the area of the wound, careful débridement of all devitalized tissue, removal of foreign bodies, and primary or delayed primary closure. In primary closure, the wound is closed without drainage. In delayed primary closure, débridement followed by packing the wound with aseptic or antiseptic gauze, or the use of the Carrel-Dakin method for four days, is availed of. If bacteriologic tests of

the wound secretions and the absence of wound reaction indicate that infection is not present, the wound is then closed without drainage.

**B. Inflammatory Period** (after 24 to 48 hours).—*Delayed primary or secondary closure.*

1. If a localized gangrenous condition occurs in the soft tissues, these tissues should be excised with the least possible adjacent traumatism. If the gangrenous process is so destructive as to render the limb useless, immediate amputation through uninfected tissue should be carried out.

2. Redness, heat, swelling, and pain indicate that the condition is becoming phlegmonous. The part should be freely opened by long incisions with the sharpest knife and with the least handling or traumatism of tissue. No attempt should be made to remove loose fragments or foreign bodies, or to débride. Ample drainage, copious wet dressings, and absolute rest are very important. Any extensive operation during this stage may result in septicemia and death. One should therefore delay the removal of foreign bodies, infection being under way, until the third or suppurating stage has become established. During the period of consolidation, from three weeks to three months after the injury, with an infected fracture, operation involving the callus is dangerous and should be deferred until sequestration has occurred.

3. A delayed primary closure not having been accomplished, and infection being present, the case can be considered only for secondary closure. The wound is freely opened, and after all dead and devitalized

tissue has been removed, very carefully treated by the Carrel-Dakin method. When practical sterility has been shown by bacteriologic tests, the soft parts are closed over the fracture.

[The successive phases in the treatment of compound fractures by modern methods may be summarized thus: (1) *First 48 hours.* Primary or delayed primary closure with débridement. (2) *Acute inflammatory period.* Simple drainage or amputation only. (3) *Suppurative period, 2d to 3d week.* Operation to remove splinters, bone fragments or foreign bodies, and to sterilize the wound area and prepare for secondary closure. (4) *Consolidation period, after 1 month.* Maintain drainage, but avoid operation until sequestration occurs. (5) *Localization of infection, sequestration and chronic purulent sinuses.* Separation of sequestra, immediate sterilization and closure by the zinc chloride or other method.

The writer's method of zinc chloride sterilization, methylene blue color delineation, and infected tissue excision will be found described in detail in Vol. VIII, under *Wounds, Septic, Treatment.* W. WAYNE BABCOCK.]

**PSEUDARTHROSIS, OR DELAYED OR NON-UNION.**—When on account of a constitutional taint (*e.g.*, syphilis), a drain on the system (pregnancy, lactation), a cachectic condition, or most commonly an imperfect reduction or inefficient immobilization of the fragments, the fibrous callus which unites the fragments fails to ossify after a sufficient length of time has elapsed, the bone formation should be stimulated by attention to the patient's general condition and such measures as will produce local irritation.

The following methods of treatment have been employed:

1. **Massage** of the overlying skin.

2. **Passive hyperemia** after the method of Bier. An elastic band is



placed around the limb above the fracture, sufficiently tight so that the part develops a warm, painless swelling. If the part below the constriction becomes cold, blue, pale or painful, the band should be removed or readjusted. This treatment, under careful supervision, may be employed from four to twenty hours daily.

3. **Tapotement.** Daily or every second or third day the zone of the fracture is struck a series of blows with a padded hammer.

4. Local irritation by blistering with a **hot iron** is of very limited value.

5. Irritation of the bone ends by **rubbing** them forcibly against each other under an anesthetic, or by the injection between the fragments of tincture of **iodine**, **Lugol's solution**, a 1 to 3 per cent. solution of **phenol**, **lactic acid**, **zinc chloride** in  $\frac{1}{2}$  to 1 per cent. solution, **turpentine**, 3 to 15 minims (0.18 to 0.9 c.c.), or best, 20 to 40 c.c. of **blood** taken from a vein in the arm, the syringe made for injecting paraffin being well adapted to this purpose. Injections of an **emulsion** made from **periosteal scrapings** and of **fibrinoplastin** have also been used.

The wearing of a **splint** loose enough to allow a slight amount of motion at the point of fracture has been advised.

**Nailing, drilling** the bone ends, stimulating **electric currents** or open **operative treatment** may be resorted to when other measures fail. In infected or compound fractures the temporary introduction of an artificial sequestrum in the form of an **intramedullary peg of boiled beef bone** may be used in association with

adequate **drainage** (Babcock) to stimulate callus formation. In the historic case of Physick union followed the introduction of the **seton** between the bone ends.

If a gap exists between the fragments it may be filled in by a **bone graft** removed from the tibia or a piece of the patient's rib, either placed in a groove cut in the bone-ends or placed as an intramedullary graft after boring out the bone-ends down to the normal medulla. In either case the graft must be in contact with living bone at each end. A gap in the tibia may be done away with by removing a section of the fibula.

To produce union in congenital pseudo-arthroses, delayed union or non-union in bones, the **osteoperiosteal graft**, plus rigid and prolonged **mechanical fixation**, as obtained by a **bone clamp**, will assure alignment and prove effective. R. T. Taylor (Surg., Gyn. and Obst., June, 1925).

The writer employed **bone implants** in 3 cases of pseudoarthrosis complicating a gunshot fracture of the jawbone. The grafts were taken from the tibia, and the usual bone grafting technic applied. Consolidation of the bone parts was manifest after 4 months, allowing mastication with artificial teeth. H. Rouvillois (Paris méd., Sept. 26, 1925).

**Nearthrosis**, a very rare condition, in which the bone-ends are separated by a joint-cavity, demands operative interference. Faulty or angular union may be remedied by **osteotomy**.

The endocrine glands are increasingly being used, **thyroid** and **parathyroid** particularly. The former may be given in 1 grain (0.06 Gm.) doses thrice daily and the latter in 5 to 10 unit doses, by injection every other day.

In rats with broken legs fed **parathyroid gland** the production of new bone at the site of fracture was doubled. Ogawa (Clin. Med., Feb., 1926).

In a personal case a fractured femur, after 6 weeks in a Hodgen's splint, showed very little callus and quite distinct crepitus. The patient was given **parathyroid** during the next 3 weeks with excellent result. J. B. Mackay (Clin. Med., Mar., 1926).

## SPECIAL FRACTURES.

### FRACTURES OF THE SKULL.

— **Varieties.**— Instead of dividing these fractures, according to their location, into fractures of the vault and of the base, it is more intelligible to speak of

1. *Circumscribed fractures*, with little injury to the brain.
2. *Fissured fractures*, usually associated with serious brain lesions.
3. *Intermediate and irregular fractures*—the intermediate fractures that combine some of the features of each of the above varieties.

**Circumscribed fractures** being usually caused by a sharp blow from some pointed object, the skull is crushed locally, without any great injury to the underlying parts. In typical cases, after the shock of the blow has passed off there is no further danger or inconvenience, except the danger of infection, for almost all fractures of the skull are compound. Sometimes the outer table alone, again (rarely) the inner table alone, and usually the whole thickness of the skull is depressed. Yet there may be no depression, the skull being simply split (locally) at the point of fracture.

The *diagnosis* may be easily made by inspection and palpation. If, however, the fracture is not compound, a ridge of clotted blood may feel like the overhanging edge of the

uninjured bone over a depression; but in the case of the clot the finger goes up one side of the ridge as well as down the other, and does not simply slide over it, and firm pressure will indent the clot, but not the skull.

**Fissured Fractures.**—These fractures are caused by the "bending" or "bursting" of the skull under pressure applied broadly. They are the "indirect" fractures of the skull, just as the circumscribed fractures are "direct." Consequently fissured fractures are much more common in the base, and circumscribed fractures more common in the vault. The bursting force may make itself felt in a radial direction or in a direction at right angles to this, and the fissures are therefore usually dispersed in one of these two directions, although the irregular thickness and elasticity of the skull, especially its base, is liable to impart to the fissure a zigzag course. The fissure may occur only at some point quite distant from the point of impact and is therefore often termed a *contrecoup*, a misleading term, for there is no *contrecoup*. On the other hand, the fissure may be so extensive as to allow the two halves of the skull to be freely movable upon each other. Since the cause of these fractures is generally a blunt instrument, they are less often compounded than the circumscribed fractures.

These fissures being due to a bursting of the skull on account of a sudden change of shape of the whole globe, it is readily understood that the associated lacerations of and hemorrhage into the contained structures are likely to be very extensive and to prove rapidly fatal, not in any sense on account of the fracture, but

on account of the trauma that caused the fracture.

**DIAGNOSIS.**—Fissures in the vault are often compounded and thus readily diagnosed. Care must be taken not to mistake a lacerated aponeurosis for a fissure of the skull. In fissures of the base, however, the diagnosis can rarely be made except by inference. As these fissures often involve the petrous portion of the temporal bone, rupturing the tympanum, hemorrhage from the ear, mouth, or nose is a fairly accurate diagnostic sign of fracture of the base. The diagnosis is, however, of very little importance.

**Intermediate and Irregular Fractures.**—Most fractures of the skull are, in a sense, intermediate between the two great divisions of circumscribed and fissured fractures, for with every sharp blow there is seen to be some compression of the whole globe, and even the bluntest force, if applied with sufficient momentum, will cause a local crushing. But an understanding of the two great classes will elucidate all such cases. Exceptionally the brain is compressed by the blood effused beneath a circumscribed fracture, and its evacuation is followed by immediate relief of symptoms; but, we repeat, such cases are exceptional.

**Punctures.**—Those which cause a local fracture are very liable to produce a local brain lesion and to lead to infection; hence they present special therapeutic indications.

**Ring fractures** around the foramen magnum are caused by a sudden blow upon the buttocks which forces the spine up into the skull, carrying a ring of the basilar portion of the occipital bone along with it.

**PATHOLOGY.**—A piece of depressed bone may lacerate both dura and pia and even the brain. In so doing it may tear the great sinuses or the middle meningeal artery. If the fracture involves the inner ear, the hearing may be permanently lost. Various nerves and vessels and the cord itself may be torn at their points of exit from the skull. Any amount of brain laceration may accompany the fracture.

**Process of Repair.**—Most of the membrane formation is done by the diploë, the osteopoietic faculties of the pericranium and dura being very slight. Consequently there is very rarely any superabundant callus, and consequently, too, if a piece of skull is removed it will be replaced only by fibrous tissue, and not by bone.

**PROGNOSIS.**—The gravity of the prognosis depends on two things, either of which may exist without any fracture at all, namely: the damage to the brain and its adnexa, and infection. The importance of depressions of small areas of the vault has been unduly magnified. Stimson strongly advises against meddling with simple depressed fractures unless focal symptoms present themselves. It is certainly absurd to suppose that the depression of a square inch of bone to the depth of half an inch or so could cause the severe and lasting shock that is so often attributed to such an injury, nor should the elevation of such a splinter be expected to relieve these grave disorders.

**TREATMENT.**—**Simple Fractures.**—Attend to the general condition of the patient and leave the fracture alone unless focal symptoms present themselves as the result of a

depression or a hemorrhage from the middle meningeal artery. In such cases operate to elevate the depression or to stop the hemorrhage. Many surgeons hold that all depressed fractures should be elevated at once. As the choice lies between the problematical danger from the existing depression and the real danger from possible infection, the question cannot be said to be definitely settled.

**Compound Fractures.**—Operate immediately for the purpose of cleansing the wound. Fill the wound itself with gauze, then shave and cleanse the whole scalp, or at least half of it. Next enlarge the skin-wound if necessary in order to catch all bleeding points and to expose the laceration of the soft parts. If there is any depressed bone it can usually be elevated by prying up the most elevated corner and extracting this piece by gentle manipulation with the forceps, after which the rest will follow easily. Occasionally the chisel or trephine may be necessary; but in all compound fractures the bone must be elevated for the purpose of assuring the asepsis of the subjacent tissues. Having elevated and removed the splinters the whole wound is copiously irrigated with "normal" salt solution. If any intracranial hemorrhage persists, the wound must be left packed with sterile or iodoform gauze for forty-eight hours, after which it may be closed. If there is no bleeding the dura is sutured if torn, and the pericranium, aponeurosis, and skin sutured in layers, the first three with catgut, the last with silk. An aluminium, silver, or celluloid plate or a sheet of goldfoil or rubber tissue

may be interposed in the gap left by the removal of fragments of bone in order to strengthen the scar.

Routine X-ray examination should be made in suspected cases of fracture of the skull. In *simple linear fractures* without symptoms, the treatment is prolonged rest; with symptoms of compression, operation for relief by: (1) removal of extradural clot with control of hemorrhage by ligation or obliteration; (2) decompression; and (3) lumbar and ventricular puncture. In *simple depressed fractures*, the treatment is operation for elevating or removing depression with or without repair of dura; relief of compression.

In *compound linear fractures* without cerebral symptoms, operation for immediate conversion of the compound into a simple fracture by excision. If there are symptoms of compression: operation for immediate conversion into a simple fracture by excision of skin and bone; relief of compression. In *compound depressed fractures*, operation for conversion into a simple fracture by excision; elevation or removal of depression; relief of compression; control of hemorrhage; repair of dura; closure of defect; and drainage, when necessary, by stab wound away from defect. W. P. Eagleton (Arch. Surg., iii, 140, 1921).

If a fissure of the skull appears in the wound, it should be thoroughly cleansed as far as infection may have traveled, the wound being slightly enlarged and the edge of the fissure chiseled away for this purpose, if necessary. There is no object in endeavoring to find the limits of the fissure, which may extend halfway around the skull or even farther. If from the force of the blow a depression of the inner table seems possible, that is no indication for increasing the patient's risks of brain infection by trephining. Such de-

pressions are extremely rare, and unless they give rise to focal symptoms they are innocuous.

Among 209 cases of fractures of the base of the skull treated expectantly the mortality was 58.3 per cent., while among 92 cases treated by operation it was 43.4 per cent. Decompression in proper cases markedly lowers the mortality. Localizing signs are no more important than the evidences of increased intracranial pressure. As a rule, the decision for or against operation can be made at once, but in some one must wait 6 to 24 hours, to observe the increase or decrease in symptoms. The pulse, temperature, blood-pressure, eye grounds should be watched. **Magnesium sulphate** by mouth or stomach tube, and an **enema** are usually given. Mixer (Boston Med. and Surg. Jour., Oct., 1917).

In compound fractures of the skull with open dura, the author advocates **excision of all traumatized tissue**, scalp, dura, and brain tissue, replacing the defect in the dura by a **transplanted** piece of **fascia**, and closing the skin completely without drainage. Sachs (Annals of Surg., Jan., 1919).

**Punctured wounds** should always be opened up, the punctured part of the skull being entirely removed by the trephine and the whole wound then irrigated and drained. Bullets located near the surface may be removed at once; if deeper and not to be touched by gentle probing, they had best be left alone, as their presence does not materially influence the prognosis. If they give rise to symptoms later, they may be located by the X-rays and their removal attempted with a greater prospect of success. Infection from the air-passages in fractures of the base cannot very well be guarded against. It is futile to render the middle ear asep-

tic when germs may constantly reach it through the Eustachian tube.

**FRACTURE OF THE VERTEBRÆ.**—The importance of fractures of the vertebræ, like those of the skull, is dependent almost entirely on the amount of damage done to the inclosed nervous tissues; on this the symptoms, prognosis, and treatment depend.

**Symptoms.**—The symptoms are mainly those of an injury to the spinal cord. If the displacement is such as to compress or tear the cord, paraplegia results, with loss of control over the vesical and anal sphincters, and in the male priapism usually occurs. Locally there is tenderness and pain, increased by motion, ecchymosis, and deformity, and crepitus in some cases.

**Diagnosis.**—Except the deformity and crepitus, any or all of the above symptoms may be caused by injury to or disease of the cord without any fracture of the spine. Hence the diagnosis is generally obscure; but no manipulation should be undertaken for the purpose of elucidating it, for fear of precipitating a fatal issue. Fracture and dislocation are usually associated, and their differentiation is of no clinical importance.

In estimating the location of the injury, it must be remembered that the pressure symptoms may be due as well to hemorrhage or inflammation as to the displaced bone, and also that it may take twenty-four to forty-eight hours for the paralytic symptoms to appear at their distinctive level. Hence the local symptoms of pain, tenderness, and deformity are much better guides to the level of the lesion than the paralytic and anesthetic symptoms.

The sensory symptoms offer the most reliable information as to when to operate. When, for instance, the anesthesia presents a line of sharp segmental limitation and does not improve within twenty-four hours, operation is advisable, as intradural hemorrhage is probably present. If, on the other hand, the anesthesia is irregular, or if it improves early, operation should be deferred, as the cord is probably not greatly injured. Operation several months after the injury, where the symptoms had been severe and had not improved, were usually futile. The operations on the spinal column are not in themselves particularly dangerous if done by skillful and experienced surgeons, and offer the best results in properly selected cases. E. D. Fisher (Trans. Amer. Med. Assoc., N. Y. Med. Jour., June 8, 1912).

**Etiology.**—Indirect violence, by causing an excessive bending of the spine, is the common cause of fracture. Such violence may be applied by a fall of the subject himself or by some heavy body falling upon him. Less frequently muscular violence produces a fracture of the spine, the usual location of such fractures being the cervical region and the usual cause a sudden jerking backward of the head: as to avoid striking the bottom when diving in shallow water.

**Pathology.**—The crushing force which causes the fracture is very likely to cause a simultaneous dislocation.

The bodies of the vertebræ are the parts most affected, except in the cervical region, where the transverse and articular processes are more frequently injured. Direct violence occasionally tears away the spinous process, <sup>Sh.</sup> There is no regularity about the sheet of gold. However, every con-

ceivable variety having been observed. The upper fragment is usually displaced forward on the lower one and the cord is compressed, rarely torn across, between the two. Subdural hemorrhage or secondary meningitis may give rise to still further compression. The nerves that make their exit at that particular segment are usually torn, as are the attached muscles and ligaments.

**Prognosis.**—*Fractures of the Lower Three Lumbar Vertebra.*—In fractures of this region only the cauda equina is liable to compression, and its individual components can usually slip aside from any obtunding fragment, and thus there will be no pressure symptoms. Under appropriate treatment the bones unite and the patient may recover entirely or with a weak back, or with paralysis or pain from pressure in some of the nerves.

*Fractures Above the Second Lumbar.*—The prognosis as regards life and death varies with the amount of damage done to the cord. If the cord is permanently damaged, the patient may continue to live as long as two months, only to die finally of exhaustion or of septic infection from bed-sores or catheterization. Death may be instantaneous from shock or from involvement of the phrenic nerve in the laceration. In fractures high up in the cervical region, even of the atlas and axis, death is not always instantaneous, but the least movement or jolt may be enough to bring fatal pressure to bear on the cord.

**Treatment.**—Experiments upon animals have shown that blows upon the cord sufficient to produce secondary edema and permanent paraplegia from degeneration may be followed by recovery if vertical in-

cisions in the bruised cord be made within a few hours after the injury.

In fracture of the spine with paraplegia, therefore, consideration should be given to an immediate **laminectomy**, with an incision 2 to 4 millimeters in depth and 2 to 4 centimeters long into the substance of the cord on each side of the posterior median fissure—provided the cord on exploration is found undivided. Immediate production of lancinating or electric-shock-like pains indicating nerve root irritation gives a hopeful prognosis from operation when unaccompanied by paraplegia. If the root symptoms are due to external hemorrhage (hematorrhachis) spontaneous improvement without operation may occur.

The onset of symptoms similar to those of syringomyelia after these injuries is suggestive of a central hemorrhage in the cord (hematomyelia) and should be treated, after careful localization, by exposure and, if possible, **incision and evacuation**. Late and persistent root pains after fracture of the spine, where there is permanent paraplegia, may be treated by **chordotomy** or by **section of posterior nerve roots**. Regeneration of the spinal cord after division or destruction does not occur, nor is it probable that regeneration of the spinal nerve roots takes place.

In traumatic paraplegia, death frequently occurs after six to eight weeks from ascending infection from the bladder. To avoid this, an attempt should be made to establish the reflex vesical arc with a **routine emptying of the bladder** at regular intervals, excited by stroking the inner side of the thigh. If retention cannot be overcome by reflex educa-

tion and infection of the bladder follows and cannot be controlled by any of the methods of catheterization, a **cystostomy** should be performed. This operation may be life-saving.

In all manipulations the greatest care must be exercised to avoid the production of further displacement. The patient must be kept upon a firm bed or rarely on a water-bed, and pressure must be taken off spots where bed-sores threaten; if they occur, they must be kept clean and dry by antiseptic powders. Nor must the patient's general vitality be neglected. As long as there is any hope of recovery **electricity** and **massage** to the paralyzed muscles are advantageous, and the strictest cleanliness must be insisted upon. The curative measures are mechanical and operative.

*Mechanical Treatment.*—This originally consisted in traction upon the head and feet by two assistants while the surgeon endeavored to reduce the fracture by direct manipulation. More recently suspension and the application of a plaster jacket, as for Pott's disease, has afforded some good results, and a similar treatment is that of Woodbury, who applied the jacket to a child upon whom traction was being made while it lay face down upon a hammock of cheesecloth. Stimson advocated suspension along a plank, the plaster being applied while pressure is maintained on the protuberance.

*Operation.*—The so-called **laminectomy** is done through a long vertical incision with its center over the fractured vertebræ. The bone is bared and the spinous processes of three or four of the vertebræ removed. Then

with rongeur forceps the laminae are divided on either side as close as possible to the transverse processes. The dura is then exposed and, if distended with pus or blood, it is incised and drained. Otherwise it is gently retracted and the bodies of the vertebrae are palpated.

Any unevenness in the vertebrae is to be removed, the straightening of the whole column attempted, and the wound closed without drainage, unless hemorrhage or suppuration demand it.

The results of operation are usually discouraging, though operation has occasionally disclosed and remedied pathological conditions upon which no manipulation could have exercised a beneficial influence.

**FRACTURE OF THE NASAL BONES.**—The nasal bones, cartilages, and septum may all be fractured. Such fractures may be followed by tedious suppuration, facial emphysema, plugging of the lachrymal canal, and, as the displacement is always backward, some subsequent deformity is inevitable, unless they are replaced.

**Diagnosis.**—By endeavoring to move the upper and lower parts of the nose laterally upon each other, false motion and crepitus will thus be elicited.

**Treatment.**—This must be begun promptly, for osseous union has been known to occur by the tenth day. By means of a director passed within the nostrils the bones are replaced. The only retentive apparatus of any value is a long pin passed directly through the nose and resting on either cheek, the nose being covered with a piece of adhesive plaster. As a general rule, however, there is no

tendency to reproduction of the deformity, and, even if such a tendency does exist, frequent reposition will appeal to the patient rather than the transfixion treatment. In old unreduced fractures an artificial bridge of aluminium, celluloid, or gutta-percha, or a cartilage transplant, may be inserted.

**FRACTURE OF THE MALAR AND SUPERIOR MAXILLARY BONES.**—Fractures of these bones, beyond the subsequent liability to suppuration and emphysema, are of no particular importance. If a fracture of the zygoma threatens a serious deformity, it may be remedied by inserting a sharp hook under the process and so elevating it. Fractures of the alveolar process of the jaw with displacement should be treated by wiring the teeth, or by the use of an interdental splint (*vide infra*).

To replace a depressed, fractured malar bone, the writer uses the ordinary cow-horn forceps of the dentist, which, in addition to sure control, has the advantage of leaving no scars, is quickly used, and does not require any opening in the mouth. The skin over the bone is suitably prepared; one point of the forceps is placed over the orbital ridge and the other just under the margin of the body of the bone at its outer side. A little pressure penetrates the skin and the points grasp the depressed bone with any degree of firmness advisable. Now the more or less impacted bone is disengaged from its bed, elevated to its proper place, and the forceps removed at once. No dressing is necessary, as the holes in the skin are mere pricks. J. G. R. Manwaring (Jour. Amer. Med. Assoc., Jan. 25, 1913).

Report of 60 cases of **bone-grafted** mandibles, of which all but 2 were free **autogenous grafts** from the ilium. Firm bony union was obtained in 56



cases, or 93 per cent. The graft and jaw fragments were so trimmed as to fit accurately end to end, with the largest obtainable areas of exposed vascular bone tissue held in close contact by firm wiring. G. Chubb (*Lancet*, July 3, 1920).

**FRACTURES OF THE LOWER JAW.**—The body, the ramus, the condyle, or the coronoid process may be fractured. Fractures of the body are, by far, the most common. They are almost always compound and occur usually in the middle line or else



Fig. 1.—Four-tailed bandage for fracture of lower jaw. (Stimson.)

are double, one on each side. Unilateral fractures are comparatively infrequent. The displacement is usually vertical and from before backward, as well. It may be appreciated by the finger inside the mouth. In fractures of the ramus there is little or no displacement. In those of the condyle that process is usually drawn forward on to the eminentia articularis, the lower fragment slipping up into the glenoid cavity and so causing the chin to deviate to that side.

The diagnosis is easy except in fracture of the ramus, where local tenderness and pain on closing the jaws may be the only symptoms.

**Treatment.**—A mild antiseptic wash should be employed frequently to lessen the danger of infection and to clear the mouth of the foul and acid discharge from the wound. Under such treatment with efficient immobilization the wound may be expected to heal kindly, though occasionally it is impossible to prevent suppuration and necrosis.

**IMMOBILIZATION.**—Though reduction is easy, the deformity tends to reproduce itself, to overcome which tendency a great number of mechanical devices have been introduced. The principal employed are external pressure, exemplified by the four-tailed bandage (Fig. 1), wiring of the bone or teeth (several on either side lest they pull out), and the interdental splint. This is a piece of gutta-percha or vulcanized rubber molded to fit between the upper and lower teeth, and of such width as to hold the jaws slightly separated so that fluids may be introduced through a hole bored in its center. This is applied and the jaw bound firmly by a four-tailed bandage. The first two methods may prove satisfactory; but the dental splint, though more complicated, is quite sure to give satisfaction if it is made by an expert dentist.

The molded lead splint introduced by Matas is most satisfactory and may be used until an interdental splint can be made.

**Bone grafting** in gunshot fractures of the mandible has involved many difficulties, but success is now the rule. Preliminary preparation is often prolonged, even for many months. When 4 to 6 weeks have elapsed since the healing of all the wounds, a curved incision is made, and a large flap raised. Fibrous tissues filling the gap between the fragments are then

cut away, the ends bevelled, a suitable graft cut from the outer surface of the iliac crest put in position, and the flap replaced and sutured. Billington, Parrott and Round (Brit. Med. Jour., Dec. 21, 1918).

### **FRACTURE OF THE HYOID BONE, THE LARYNX, AND TRACHEA.**

—These rare fractures are usually caused by direct violence, as in strangulation. They may be recognized by direct palpation. They endanger life by obstructing respiration. If the symptoms are urgent, tracheotomy should precede attempts at reduction.

**FRACTURE OF THE STERNUM.**—This accident is very rare. It is usually caused by the strain of bending forward or backward. The symptoms and treatment are those of dislocation (*q.v.*).

**FRACTURES OF THE RIBS.**—These are frequent, though often multiple, and occur usually between the fifth and ninth. The upper and lower two ribs are almost never fractured. In single fractures there is, as a rule, no displacement; but multiple fractures may give an angular displacement, or, if sufficiently extensive, a caving in of the whole side of the chest. The fracture may be located by a localized point of tenderness (and crepitus), which may be elicited by pressure on the shaft of bone at a distance from the fracture. Crepitus may also sometimes be elicited by deep inspiration, which is painful. If the lung is pierced there may be cellular emphysema, hemothysis, and later a pneumothorax.

**Treatment.**—Displacement having been corrected, the bone is immobilized by strapping the chest with adhesive plaster. During expiration

a strip of plaster two inches broad is applied, beginning over the sternum and following the curve of the ribs over the point of fracture, and around to the opposite axilla. If several ribs are broken they are covered from above downward by similar strips overlapping.

It is necessary to watch fractures of the ribs carefully for a couple of days to note the onset of pulmonary complications. Localized pneumonitis sometimes occurs. In strapping the chest for fractured ribs, the straps should pass well beyond the median line. They should be applied during full expiration. One or two straps passed over the shoulder help much to secure immobilization. Fuld (Internat. Jour. of Surg., June, 1912).

**FRACTURE OF THE COSTAL CARTILAGES.**—See DISLOCATIONS.

**FRACTURES OF THE CLAVICLE.**—They are very frequent in children, being caused by a fall upon the arm which in an adult would be more likely to dislocate the shoulder. They occur usually in the middle third of the bone, are not infrequently incomplete, but very rarely compound.

Fractures of the middle third are transverse or oblique, from above downward and inward. The shoulder, losing its anterior support, drops downward, inward, and forward; the posterior border of the scapula is raised outward and its lower angle rotated slightly upward and backward. If the fracture is oblique the outer fragment slips below and behind the inner one, whose edge is prominent under the skin. Transverse fracture may give rise to angular deformity, the angle pointing upward and backward. If the fracture is comminuted the small fragments are

markedly displaced; if it is bilateral the weight of the two shoulders on the chest may cause urgent dyspnea (relieved by dorsal decubitus). Injuries to the great vessels, nerves, and lungs are rare complications. The arm can be moved forward or backward, but cannot be abducted on account of the pain rather than the muscular disability.

In fractures of the outer third the line of fracture is usually transverse

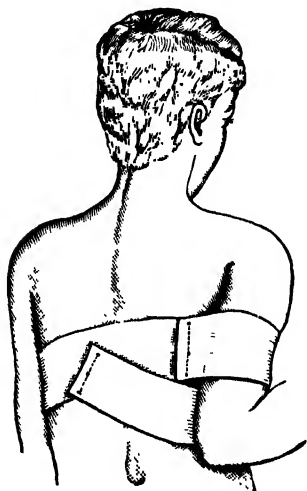


Fig. 2.—Sayre's adhesive-plaster dressing for fracture of clavicle. First piece. (Stimson.)

and the displacement angular, with the apex backward. Disability and deformity are not great.

In fracture of the inner third the outer fragment passes below the inner one or is accompanied by it, producing angular deformity.

**Prognosis.**—Union is almost certain to take place at the end of four weeks whether the fracture is immobilized or not. Some persistent displacement is the rule, especially in adults.

**Treatment.**—Reduction is effected by pushing the shoulder upward, outward, and backward. Manipulation

of the arm or simple dorsal decubitus will effect this. To maintain perfect reduction dorsal decubitus with the head slightly raised and the forearm resting across the chest is usually essential. In the green-stick fractures of children a simple sling may be sufficient, and the same dressing may be applied to all patients who are impatient of restraint in the more complicated dressings and are willing to accept the subsequent deformity.

In other cases Sayre's or Velpeau's dressings will produce an esthetically satisfactory result.

**Sayre's dressing** (Figs. 2 and 3) requires two strips of adhesive plaster, each three inches broad and long enough to reach one and a half times around the body. The end of one strip is fixed loosely about the arm on the injured side just below the axilla. It is then carried around the back and across the chest in such a way as to hold the elbow a little behind the axillary line. The other strap is then carried from the uninjured shoulder across the back and the point of the elbow and back to the point of starting, carrying the elbow forward, upward, and inward. Thus the shoulder is carried upward, outward, and backward. The axilla and the whole inner surface of the arm and forearm should be well padded with cotton or wool, and the bony points of the elbow should be protected in like manner. The band had best be left uncovered and the whole dressing supported by a few turns of a roller bandage.

A simple treatment for fractured clavicle with displacement is described by the writer. He passes between the elbows and the back a **bar or board thickly padded** in its central portion and left thinner laterally. To hold this bar

in position a broad bandage is passed around its central portion, then up like suspenders over the shoulders, diagonally across the chest anteriorly, underneath and around the forearm of the opposite side, then directly upward to the clavicle of the same side, where it is pinned to the previous turn over the shoulder. At night the patient remains in a half sitting posture, enough pillows being placed under the back to keep the elbows off the bed. Senlecq (Paris méd., Mar. 29, 1919).

The writer employs a 3-piece plaster cast. One cast surrounds the chest, another is a movable unit around the arm, and the third overlaps the other 2 for purposes of firm and precise adjustment. W. L. Bell (Annals of Surg., Nov., 1922).

Velpeau's dressing, as shown in Fig. 4, holds the elbow pressed against the front of the chest. It is made with a roller bandage. Padding should be applied as noted above.

Moore's ingenious combination of a posterior figure-of-8 bandage to both shoulders and one elbow with a sling (Figs. 5 and 6) is effective, but uncomfortable, and unless carefully padded is likely to interfere with the circulation of the arms.

Fracture of the outer third is best immobilized by Stimson's dressing for dislocation of the outer end of the clavicle (*q.v.*).

To avoid deformity displaced comminuted fragments may be removed through a small incision.

**FRACTURES OF THE SCAPULA** are divided into fractures of the body of the lower angle, of the spine, of the acromion, of the coracoid process, of the surgical neck, and of the glenoid fossa.

**Fractures of the body and inferior angle** may be partial or complete,

simple or comminuted. When the angle is torn away it is drawn forward by the attached muscles and cannot be replaced. In fractures of the body displacement is usually confined to overlapping of the fragments. The diagnosis is made in either case by palpation, and the sole treatment is immobilization by plaster strapping, as for fractures of the ribs, and support of the arm by a sling. The only complication to be feared is suppura-



Fig. 3.—Same as Fig. 2. Second piece. (Stimson.)

tion in the deeper planes, which may follow even a simple fracture if the contusion has been severe.

**Fracture of the acromion** may be caused by external violence acting directly or through the humerus, or else by contraction of the deltoid. The fracture is usually beyond the attachment of the clavicle. Non-union of the epiphysis may occur. Bony union can rarely be obtained, but no disability follows fibrous union.

**TREATMENT.**—Velpeau's dressing (Fig. 4).

**Fracture of the coracoid process**

may be caused by external violence or muscular action and is often complicated by other injuries. Abnormal mobility, with or without crepitus, may be obtained by pressure on the tip of the process. Fibrous union without disability is the rule.

**TREATMENT.**—Treatment is by immobilization of the arm in slight hyperextension.

**Fracture of the Surgical Neck.**—Either the whole of the glenoid fossa or only a part of it is torn off with the long head of the triceps attached to



Fig. 4.—Velpeau's dressing for fracture of clavicle. (Stimson.)

the fragment. The support of the triceps being lost, the whole shoulder sinks downward and the displacement resembles very closely a subcoracoid dislocation. The arm, however, is not abducted nor is there any characteristic restriction of motion; a lump may be felt in the axilla, and the deformity may be reduced (with crepitus) by lifting the arm, but immediately recurs.

**TREATMENT.**—The treatment is as for dislocation of the clavicle; bony union may be expected.

**Fracture of the Glenoid Fossa.**—The rim is often broken, with dislocations of the shoulder-joint. Stellate

fractures have been found *post mortem*.

**FRACTURES OF THE HUMERUS.**—These may be conveniently grouped into fractures of the *upper extremity*, of the head, anatomical neck, through the tuberosities, of either tuberosity, of the surgical neck; and separation of the epiphysis, of the *shaft*, and of the *lower extremity*; supracondyloid, intracondyloid, of either condyle, or epicondyle; and separation of the epiphysis.

**Fracture of the Head.**—This is very rare, excepting the splitting that may accompany dislocation, and cannot be recognized clinically.

**Fractures of the Anatomical Neck and Through the Tuberosities.**—These present the same clinical features and can rarely be differentiated before death; indeed, the line of fracture is likely to be so irregular as to be partly through the neck and partly through one or other tuberosity. These lower fractures are certainly more frequent than simple fractures of the anatomical neck. Most cases occur in connection with anterior dislocation. There may or may not be impaction. If the head is dislocated forward it may be felt, and its independent mobility recognized when the shaft of the bone is rotated. If the head is not dislocated, pain in upward pressure on the elbow may be the only symptom.

**TREATMENT.**—If the head is not dislocated, treatment is by immobilization with slight traction. If it is dislocated, alternatives present themselves: The surgeon may maintain the two fragments in apposition, hoping to obtain union, and then at the end of five weeks to attempt reduction by manipulation, or, this

failing, by operation. On the other hand, he may, and this seems the better plan, attempt reduction at once. If his manipulative efforts do not succeed, he may attempt operative reduction, laying bare the head, boring a hole in it, and then reducing it by means of a stout right-angled hook (McBurney) inserted into this hole. Failing in this, he may exsect the head. In any case the area should be immobilized for five weeks. The theory that the head subsequently atrophies has no very good foundation in fact. On the contrary, very good functional results are obtainable.

**Fractures of the tuberosities** occur in connection with dislocation of the shoulder forward (greater tuberosity) or upward (lesser tuberosity). As the fracture is often incomplete, bony union without much deformity is the usual result.

**Separation of the epiphysis** may occur at any time during the first two decades of life. The most common mechanism of its production is probably hyperabduction in the efforts to pull down the arm during labor. The line of separation runs just below the tuberosities and the usual displacement is of the lower fragment more or less completely to the inner side and in front of the upper one, which is tilted outward. The edge of the lower fragment may be felt or even seen close under the skin in front. Crepitus is slight, owing to the cartilaginous nature of the edges. Reduction is by manipulation or by forced abduction, which brings the lower fragment in line with the upper one. Union may be irregular if the periosteum slips between the fragments. Immobilization must be maintained for five weeks. Persistent displace-

ment or premature ossification of the epiphysial cartilage may arrest the growth of the limb.

**Fracture of the surgical neck** is by far the most common of the fractures of the upper extremity of the humerus. Under this head are classed all fractures between the line of the epiphysial junctures and the insertion of the pectoralis and teres major. They are caused by direct violence or

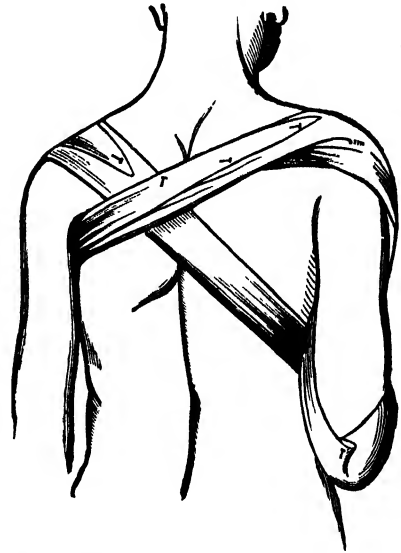


Fig. 5.—Moore's dressing for fractured clavicle.  
(Stimson.)

a fall upon the elbow. The displacement is usually slight, but the lower fragment may be drawn up and to the inner side of the upper one, which is then held in abduction. The diagnosis is made by eliciting abnormal mobility and crepitus when the tuberosities of the humerus are firmly grasped and the arm gently rotated. In impacted fractures there is a tender spot just below the tuberosities and the arm is usually held in slight abduction.

**TREATMENT.**—If there is much overriding, reduction can only be effected

by traction in extreme abduction. The Thomas traction arm splint or the Jones humerus splint or their modifications are of great value. If the fragments are impacted in fair position, or if there is no displacement, as is often the case, any immobilizing dressing will be sufficient. Usually, though, there is some tendency to shortening to be overcome by traction and often some abduction in the upper fragment that cannot be overcome. To meet these indications various splints have been devised. For abduction of the upper fragment the best treatment is generally to keep the patient in bed and traction by weight and pulley (see FRACTURES OF THE THIGH) on the arm held in partial abduction by being bandaged on a triangular pad or a bent metal band fitted into the axilla. After two weeks sufficiently firm union will probably have taken place for the arm to be abducted. In this position it is maintained for three or four weeks longer, by a plaster mold or circular splint of which the upper edge is molded well over the shoulder to immobilize the joint, and which is made light over the forearm (the elbow being bent to a right angle) and heavy over the arm. The whole is bound lightly to the chest and the wrist above supported by a sling, in order that the weight of the arm may tend to prevent shortening. Any shortening that may occur will be indicated by a rising of the shoulder-cap and must be compensated by weights attached to the elbow. During all this time frequent exercise of the wrist and fingers must be insisted upon.

A variation of the above line of treatment should be effective in any

case. Ambulatory treatment with the arm in abduction is possible, but irksome.

A simultaneous dislocation of the head is treated as above indicated.

The *position of fixation* for fractures of the shoulder girdle and upper third of the humerus should be with the arm in abduction of 90° and the hand midway between pronation and supination. The elbow may be flexed

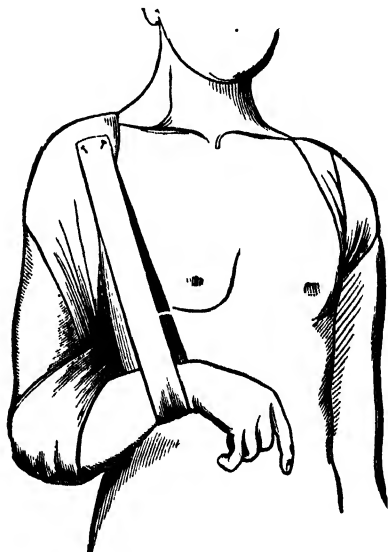


Fig. 6.—Moore's dressing for fractured clavicle.  
(Stimson.)

or extended according to the particular case.

**Fractures of the Shaft.**—These are caused by external violence or by muscular action. All varieties of fractures and displacements are seen here. The vessels or nerves may be injured, notably the musculospiral, which may be torn across, pressed upon by the callus, or caught between the fragments. Union is more likely to fail in this than in any other bone: a fact that has been explained by deficiency of immobilization, for, since the hand is supported by a

sling every motion of the head and neck imparts a slight movement to the fragments.

The treatment is along the same lines as that of the surgical neck. Shortening must be carefully watched for and prevented.

**Supracondylar Fracture.**—The line of fracture passes through the lower part of the humerus, just above the condyles. The joint is usually not involved, but may be opened by an additional intercondylar fracture or fracture of the olecranon. The line of fracture is usually from behind downward and forward, and consequently the lower fragment is displaced upward and backward. The sharp point of the upper fragment may pierce the skin in front; more rarely the fracture is compound from behind by the lower one. If the swelling is not too great the displacement can be seen as well as felt, and false motion and crepitus elicited by moving the condyles on the shaft. Dislocation is ruled out by the normal relation of the olecranon and epicondyles, as compared with the other arm, and intercondyloid fracture by the absence of its typical symptoms (*q.v.*).

**TREATMENT.**—Same as for fractures of the lower part of the shaft: immobilization with the elbow flexed at a right angle and the forearm in semipronation. A sufficient weight, usually five pounds, should be suspended at the elbow to prevent shortening, and the *hand alone* suspended in a sling.

Treatment by extension may be advantageously combined with suspension of the limb in a vertical position for the first fortnight of treatment of a compound fracture.

As a result of the "no splint" treatment of fractures about the shoulder, in the humerus, and the elbow it is possible for a patient to return to work in 6 or 8 weeks.

For 10 years the author has been treating fractures in these regions without splints and has never been disappointed.

All fractures are treated with the arm in a sling, plus a posterior splint with a lower projection for the first few nights.

In 3 or 4 days **passive movement** is begun, and later **active movement**. J. W. Dowden (Edinburgh Med. Jour., xxi, 328, 1918).

**Suspension treatment** of fractures of the humerus promotes more rapid union and earlier restoration of function. It does not require nearly so much skill as does treatment by splints. The so-called **Balkan frame** is excellent for the purpose, but a gallows frame consisting of a post and arm is sufficient. In applying the treatment vertical suspension of the forearm is secured by bands glued to the skin and attached by straps and buckles to a wooden spreader. A round wooden handle is attached by pieces of elastic webbing to the ends of the spreader, thus enabling the patient to exercise the fingers. The arm is suspended horizontally by a broad sling of duck, muslin, or rubber sheeting, one end of which is tacked to one side of a wooden spreader while the other end is pierced with eyelets which hook over hooks on the other side of the spreader, so that the sling can be reduced for dressings. Traction on the arm in case of high fracture is made by bands glued to the skin of the arm and attached by buckles and straps to a wooden spreader; in low fractures by a double band of muslin 6 cm. wide; fastened about the padded arm just above the elbow. Equal weights, averaging three pounds, are used for the arm and forearm, though eight pounds is used at first until reduction has occurred. J. A. Blake (Amer. Jour. of Surg., May, 1921).



**Intercondyloid Fracture (T- or Y-fracture).—**This differs pathologically from a supracondylar fracture only in the additional line of fracture separating the condyles. The additional force usually required to produce such a fracture is such that the displacements are varied and likely to be marked, and the fracture is often compound and associated with injuries of the adjacent vessels and nerves. In doubtful cases the characteristic symptoms to be sought for are mobility of the condyles upon each other, usually with crepitus, and, in still more obscure cases with no displacement, simple tenderness when the two condyles are pressed against each other.

**TREATMENT.**—The treatment is that of supracondylar fracture with additional care in the immobilization of the fragments. Anterior and posterior plaster splints are usually satisfactory. In compound fractures, where the joint is widely laid open, Kocher advises the removal of the external condyle to facilitate drainage and to produce a fairly strong and movable joint. In some cases it may be necessary to remove both condyles with the risk of substituting a flail joint for an ankylosed one. In all compound fractures the fragments should, of course, be retained in place, by suture or temporary pegging with a nail or drill.

**Fracture of the Epitrochlea, or Internal Epicondyle.**—This occurs in connection with dislocation of the elbow or as the result of direct violence. The fragment is left more or less closely attached to the condyle and its mobility may be readily recognized. Paralysis and neuralgia from pressure on the ulnar nerve have been

known to follow this fracture. A spontaneous cure may generally be expected.

**TREATMENT.**—Direct pressure with immobilization of the forearm in flexion to relax the attached muscles. Two or three weeks' treatment suffices.

**Fracture of the External Epicondyle.**—This is caused by direct violence and is extremely rare. The mobile fragment is easily recognized and immobilized.

**Fracture of the Internal Condyle.**—This is caused by indirect violence through forcing upward the condyle with the ulna attached to it. The line of fracture runs from the inner side of the humerus downward and outward to the center of the trochanter or between it and the capitellum. Ligamentous attachment to the ulna usually prevents any marked displacement, and the swelling all about the joints usually obscures such displacement as there is. The forearm is adducted, however, and abnormal adduction and abduction are possible at the elbow. (These movements can only be distinguished from rotation of the humerus when the joint is in full extension: a position but rarely obtainable except under anesthesia.) Independent mobility of the fragment and tenderness on transcondylar pressure should be sought for. Coincident dislocation of the radius backward from the external condyle leaves that part of the humerus prominent anteriorly (see DISLOCATIONS). Unless such dislocation is present, the altered relations of the epicondyles and olecranon are likely to be distinguishable through the swelling.

The treatment is by immobilization in the usual semiflexed position. The

positions of extreme flexion or extension which have been advocated are inconvenient and present no advantages. If the fragment will not remain in place, it must be cut down upon and fixed by suture. Angular deformity is liable to ensue from suspension of the elbow, as in supracondylar fracture, and may occasionally follow premature ossification of the epiphyseal cartilage after fracture of the internal condyle in the adolescent. Excessive formation of callus is likely to impair the functions of the joint, especially in the young.

#### **Fracture of the External Condyle.**

—The fragment consists of the external condyle, the capitellum, and part of the trochlea. The symptoms are the same, *mutatis mutandis*, as those of fracture of the internal condyle, but the disability is usually less. As more or less rotation of the fragment is liable to occur, the most difficult part of the treatment is reduction, for which an operation may be necessary. Under such circumstances Kocher has excised the condyle, with good results.

After the reduction has been accomplished there is little difficulty in retaining the fragment in place, and three weeks in a posterior molded splint with the joint at midflexion suffices for a cure. Excessive callus may interfere with the function of the joint.

**Separation of the Epiphysis.**—This accident is very rare. The epicondyles may or may not remain attached to the upper fragments. The chief symptoms are pain on pressure of the forearm against the arm, abnormal mobility, and cartilaginous crepitus. The treatment is the same as that of supracondylar fracture.

**Subepicondylar Fractures.**—These usually involve both trochlea and capitellum, very rarely the trochlea alone. If there is no deformity, the fracture may be trusted to heal under immobilization. But if there is persistent displacement the fragment or fragments should be excised. The fluoroscope may be of great assistance in diagnosing obscure lesions about the elbow-joint, but most cases can be diagnosed and treated without its aid.

**After-treatment of Fractures about the Elbow.**—After the three or four weeks that are necessary to obtain union of the fracture, the elbow will be found quite stiff. If this stiffness is due solely to adhesion and capsular retraction, it may be expected to disappear after some weeks of natural use of the limb. Excessive callus, too, will diminish rapidly, and it is doubtful whether any treatment will hasten its absorption. Forcing of the joint is harmful, as a rule, and if convalescence is too slow elastic traction to increase flexion and a weight on the hand to increase extension may hasten matters a little by supplementing the patient's own efforts. Osteotomy or arthrotomy may be resorted to after several months have elapsed; but the more conservative the treatment, the better will be the results.

#### **FRACTURES OF THE RADIUS AND ULNA.**—**Fracture of the Olecranon.**

—This may be at the tip or near the base. The mechanism is usually indirect violence combined with the action of the triceps, the olecranon being broken across the trochlea as a stick would be across one's knee. Aponeurotic and periosteal lacerations are usually slight, and consequently there is little or no

displacement. The mobility of the fragment is readily recognized.

**TREATMENT.**—If the displacement is slight, and is not increased by flexion the elbow may be immobilized midway between full extension and flexion at a right angle. In other cases the elbow must be retained in full extension, and it may even be necessary to pull the olecranon down. The simplest method of traction is by a narrow strip of adhesive plaster running up the side of the forearm over the upper border of the olecranon and down the other side. In cases with separation of the fragments open operation and suture of the torn triceps expansion is indicated. An anterior molded splint gives satisfactory immobilization and permits observation of the displacement. Union is likely to be fibrous, and, in those cases in which this greatly impairs the use of the limb, the fracture may be freshened and sutured.

**Fracture of the coronoid process** is extremely rare except as a complication of dislocation. As the brachialis anticus and capsule are attached to the bone below the process, its displacement is slight and it unites kindly under immobilization at a right angle (to prevent recurrence of the dislocation).

**Fracture of the head and neck of the radius** are much more common than was formerly believed. Of 29 cases which came under the observation of Hitzrot, 19 involved the head and 10 the neck.

In 15 cases of *fracture of the head* there was but little displacement of the fragments. In 4 cases the fragments were displaced anteriorly.

The disability was rather characteristic in all types. The arm was

held in flexion midway between pronation and supination and both the latter movements were impossible. Pain was markedly increased by abducting the arm and pressing over the head of the radius, and especially so, if pronation and supination were attempted in the above position with the above pressure.

**TREATMENT.**—In the writer's 15 cases without displacement the arm was supported by a posterior splint, **baking** begun on or before the third day, and **massage** before the second baking, i.e., on the fifth day. Movements in flexion and extension were begun as soon as the swelling subsided, usually about the tenth day. Pronation and supination were begun about the fifteenth day. Result: Flexion and extension were complete in all the cases. In 2 cases (chipping off of the radial side of the head) pronation and supination were so slightly altered as to be classed as perfect. In 11 cases pronation and supination were half of that on the normal side. In 2 of the same type as the first 2 mentioned cases, but with the line of fracture beginning well to the ulnar side of the articular surface of the head and extending outward through the head, supination was one-quarter and pronation one-half normal. Both the latter cases have some pain during pronation and supination.

In the 4 cases with displacement of the fragments the X-ray was necessary for diagnosis of the displacement. In 2 the head was broken into three fragments, two of which were displaced anteriorly while one fragment remained in position. In this type the entire head was removed by cutting through the neck about one-

half inch below the articular surface of the head and removing the head.

In the remaining 2 cases the head was broken in one place only and the fragment which was radially placed was displaced outward and forward, and in this type the fragment only was removed.

The after-treatment was similar in other respects to that pursued in the fractures without displacement.

**Result:** The resulting motion was better in those cases in which the head was removed and better in that case in which the most bone was removed (*i.e.*, the neck cut through at the lowest possible level). In the last mentioned case supination was present to seven-eighths the normal and pronation was complete. In the other case of complete removal, supination was two-thirds normal and pronation seven-eighths normal.

In the 2 cases of partial removal of the head supination was one-half normal, pronation two-thirds normal, and pain was present during either movement in 1 of the cases for nearly a year.

The 10 cases of fracture of the neck of the radius were all transverse in type and involved that portion of the shaft about one-half inch below the head. The X-ray was used to confirm the location of the fracture, and in none of the cases was there any marked displacement.

With the arm in the midposition between pronation and supination a U-shaped plaster splint (see fractures of both bones of forearm for details) was applied and left on for from three to five weeks. **Massage** was begun on the tenth day and **passive motion** and rotation at the end of the third week.

Pronation was complete in 2 cases and in these 2 supination was also nearly complete. In the other 8 cases pronation was two-thirds normal and supination five-eighths normal.

**Fractures of the Shaft of One or Both Bones.**—Fracture is usually in the middle or lower third of the forearm, and the radius is usually fractured at a higher level than the ulna. Fracture of a single bone is most frequently due to direct fracture of both bones to indirect violence. Greenstick fractures are more common in the radius than in any other bone. Displacement in any direction may occur, and, if unreduced, is of special importance as affecting the rotation of the forearm. A peculiar displacement is that of supination of the upper fragment of the radius by the biceps when the bone is broken above the insertion of the pronator teres. According to most authors, unless the limb in such case is immobilized in extreme supination a permanent loss of that motion will result. Practically, however, the impairment to supination when the limb is kept in the usual semipronated position is unimportant. Of far greater importance is the total loss of rotation that follows fusion of the two bones even when a lateral enarthrosis appears in the callus, as is rarely the case. The points that favor such a fusion are: (1) persistent displacement of the bones toward each other, (2) excessive callus from insufficient immobilization or imperfect reduction, and (3) the rare occurrence of fracture in both the bones at the same level.

In fractures of a single bone the displacement is usually slight, and the diagnosis may be difficult. A point of local tenderness may be

found with either crepitus, false motion, or irregularity of the surface of the bone. In fractures of the ulna alone the head of the radius is often dislocated forward and upward.

**TREATMENT.**—Reduction by traction and local pressure, special attention being paid to the correction of any displacement of the bones toward each other, forcing them apart by deep pressure with the finger-tips on the front and back of the forearm. Greenstick fractures must be reduced by forcible bending, even completing the fracture, if necessary. *Circular constriction* of the limb should *never* be applied, for this is a most fruitful source of gangrene. The arm should be placed midway between pronation and supination with the elbow flexed to a right angle.

The best splint is a U-shaped molded plaster splint, which should begin at the base of the fingers on the palmar side, pass up the anterior surface of the arm about the flexed elbow, and down the dorsum to the base of the fingers. This is carefully bound in place, avoiding circular constriction. The patient should be encouraged to move the finger from the start. Firm union occurs in from six to fourteen weeks, but delayed union is quite frequent.

In fractures of the ulna at its upper third with dislocation of upper end of radius the writer urges the abandonment of simple arthrotomy or excision of a portion of the radius in this condition, and advises treatment as follows: In recent cases reduction without operation should first be attempted. The joint should be immobilized in the acutely flexed position and two radiograms from different aspects taken. If the radial head is not in place, or if there is overlapping or angular displacement of the ulna, which would prob-

ably later hinder supination and pronation, operation after at least a week has elapsed is indicated. J. Abadie (*Presse méd.*, Jan. 18, 1913).

The writer argues against the customary immobilization of elbow fractures in children in plaster casts for 3 weeks. Reduction and fixation can nearly always be effected more easily and completely in the extended position. This permits ready reduction of lateral displacements and even of co-existing dislocations. Consolidation takes place so rapidly that in 10 days flexion can be substituted and the joint then immobilized again for 10 days. Complete mobility of the elbow is thus preserved and recovery of function hastened. The author reports 35 successful cases. Mayet (*Presse méd.*, Jan. 7, 1918).

Many deformities follow in these cases because of reluctance to put patients to bed. **Traction** is essential. **Suspension** of the forearm in the perpendicular position, with the elbow flexed at right angles, is the most satisfactory position. In **operative treatment**, the site of election for incision is lateral, either on the radial or the ulnar side, or both. Fingers and hand should be moved regularly and systematically as soon as possible. Magnuson (*Jour. Amer. Med. Assoc.*, Mar. 18, 1922).

**Fractures of the Lower End of the Radius (Colles's Fracture).**—This is, after fracture of the ribs, the commonest of all fractures. It is generally produced by a fall upon the palm of the hand. The line of fracture runs irregularly across the bone within an inch of its articular edge. In the young it commonly follows the epiphysial line. The lower fragment is tilted back and impacted. It may be comminuted. The upward displacement is not great, but the tilting and crushing carry the styloid process of the radius to a higher level than that of the ulna, which is made promi-

nent by the shifting over of the carpus. The periosteum on the back of the radius remains untornd. The styloid process or shaft of the ulna may be broken. Rarely the internal lateral ligament is torn.

The characteristic symptoms are the so-called "silver-fork" deformity—a backward displacement of the whole hand and the lower end of the radius, producing a swelling over the back of the wrist and a deep crease in the front. The styloid process of the ulna is prominent and lower than that of the radius. Crepitus and mobility are usually absent. There is a line of tenderness along the line of fracture.

Automobile fractures are cases of fracture of the lower and usually outer end of the radius caused by the sudden and violent reversal of the starting crank of an automobile, the so-called "kick-back." Only those produced indirectly by the force acting through the palm of the hand are meant. The X-ray picture in a typical automobile fracture will show a fracture line in the lower end of the radius below the usual site of a Colles fracture. This line runs either transversely across the bone or, what is more common, obliquely into the joint. There is no impaction, no displacement, and consequently little or no deformity. There is, as a rule, no crepitus, little deformity, swelling, pain, or discoloration. The loss of function also is slight, though rather greater than the other clinical symptoms would call for. Gentle motion can be made; forced ones are painful. There is a distinct point of tenderness on the lower and outer end of the radius, and this clinical sign is always present and shows, in this fracture perhaps more than any other, the value of pressure-point tenderness in the diagnosis of fractures. The diagnosis must often be made from the history and this sign alone. An X-ray is to be taken when possible. In regard

to treatment, the less done the better, as a rule. Any attempt to improve the slight deformity is unnecessary. The author's cases proceeded to a speedy and full functional recovery without any manipulations. He recommends **immobilizing**, and, after a week, daily **massage** and **motion** of the joint. Recovery is usually complete in three weeks. W. H. Winterberg (Calif. Jour. Med., Feb., 1912).

In an analysis of a series of 3785 forearm fractures that had been roentgenographed in the Howard and University of Pennsylvania Hospitals, the writer found that over 7 per cent. were due to backfire. Of these the so-called Colles headed the list, constituting 27.6 per cent. of the total number, while the so-called chauffeur fracture (styloid of the radius) amounted to 25.2 per cent. of the number. Eliason (Jour. Med. Soc. of N. J., Mar., 1925).

The diagnosis from dislocation is given under that heading.

**TREATMENT.**—The simplest way to break up the impaction is for the surgeon to grasp the forearm firmly just above the fracture. With the other hand he then grasps the injured hand, placing his thumb lightly on the back of the lower fragment. Dorsal flexion is made until the patient complains of pain, and then with a sudden movement the dorsal flexion is increased and simultaneously strong pressure is made on the lower fragment. In a moment the fracture begins to give, the dorsal is quickly exchanged for palmar flexion, the wrist being pried backward, and the resultant crepitus announces the dissolution of the impaction.

Inspection should thereupon show that the "silver-fork" deformity has disappeared. The impaction once thoroughly broken up, the bones tend to remain reduced, and should be immobilized by anterior and posterior

plaster splints, which need not extend so far up the forearm as for fractures of the shaft (*q.v.*). **Massage** is very useful to shorten the convalescence and can best be used if, instead of wooden splints, molded plaster ones are used, extending from the middle of the forearm to the metacarpophalangeal joint both in front and behind. The hand is most comfortable in slight dorsal flexion.

Always anesthetize the patient and adjust the fragments so that soft structures within the annular ligament will be freed from compression. Apply a short and light molded splint of cardboard posteriorly and a small loose roll of gauze anteriorly. If this does not hold the fragment nicely in place, add a cardboard splint anteriorly. After 3 weeks remove the splints but retain the sling for another week. Also after 3 weeks excite a **Bier's hyperemia** daily with the rubber bandage, or by plunging the hand and wrist alternately into hot and cold water for 5 minutes morning and night. Add **massage** as long as seems desirable. R. T. Morris (N. Y. Med. Jour., Jan. 6, 1917).

The writer's personal method of reduction is to reverse the mechanism of the production of the deformity. Thus, if the ulna is the fixed point about which the hand is displaced, it is made the fixed point about which one reduces; if the hand is displaced in extension, it is reduced in flexion, and if it is displaced in a rotation of supination about the ulnar head, it is reduced in pronation. After the obvious displacement of the radius is corrected, the hand is carried about the ulnar head as a fixed point into pronation and flexion. A good deal of force is directed up under the ulnar head, a strong force flexes the hand, and a twist of the whole hand about the ulnar head finishes the work. The average splints are often inefficient. The position is best held in flexion, and flexion is best held in plaster, pre-

ferably applied as strip splints of 8 to 10 layers of plaster-of-Paris bandage, 1 on the back from elbow to finger knuckles, 1 in front from upper forearm to palm, these caught with a few turns of plaster bandage. One should watch carefully for interference with circulation, if necessary slitting the plaster after a day or two. The flexed position is abandoned after a fortnight and straight splints then worn for a week. F. I. Cotton (Boston Med. and Surg. Jour., Dec. 4, 1919).

#### Other Fractures Near the Wrist.—

Cases have been recorded of reversed Colles's fracture from a fall on the back of the hand. The lower end, or styloid process, of the ulna may be fractured alone. The so-called Barton fracture of the anterior or posterior lip of the articular surface of the radius is merely incident to dislocation of the carpus (*q.v.*).

**FRACTURES OF THE CARPUS.**—Since the advent of the X-ray, fractures of the carpal bones are found to be more common than was formerly supposed. Of these fractures, fracture of the scaphoid and fracture of the scaphoid with dislocation of the semilunar are the most common. Fractures of the os magnum, semilunar, trapezium, cuneiform and pisiform are rare and an X-ray picture is needed for diagnosis.

#### Fracture of the Carpal Scaphoid.—

**ETIOLOGY.**—A fall or blow upon the ball of the thumb with the wrist in dorsal flexion.

**PATHOLOGY.**—The line of fracture is transverse and usually nearer the proximal portion of the bone. The fragments are more widely separated in ulnar flexion and closer together in radial flexion of the hand. When one fragment is displaced it is usually the proximal fragment and the displacement is anterior.

**SYMPTOMS.**—Pain in the wrist-joint, limitation of all movements, swelling and tenderness upon digital pressure in the anatomical snuffbox between the thumb extensors, especially in radial flexion of the hand.

**DIAGNOSIS.**—The X-ray is necessary to confirm the diagnosis.

**PROGNOSIS** should be guarded. As a rule, there is some limitation of motion and pain on long use.

**TREATMENT.**—In cases without displacement, a palmar splint with hand in radial flexion, early **massage**, and **baking**.

Where the proximal fragment is displaced, incision and removal.

**Fracture of the Scaphoid with Dislocation of the Semilunar.**—The cause is the same as that of scaphoid with some additional force pressing the hyperflexed hand either directly or obliquely toward the radius.

**SYMPTOMS.**—Pain, disability, tenderness in the snuffbox, and a hard, bony swelling beneath the extensor tendons; shortening of the wrist, and radial deflection of the hand and prominence of the lower end of the ulna.

**TREATMENT.**—Excision of the semilunar and displaced proximal fragment of the scaphoid.

The prognosis and after-treatment is the same as in fractures of scaphoid.

**Metacarpal Fractures.**—The base of the first metacarpal is frequently broken (Bennett's fracture) and is easily recognized.

The other metacarpal fractures usually occur in the third and fourth bone and are caused by direct or indirect violence. The injury is readily recognized. The tendency to displacement is slight.

The X-ray has demonstrated the comparative frequency of fracture of the metacarpal bones. This is especially noteworthy in boys under 18, in whom there is frequently a separation of the epiphysis due to direct violence. Cases of fracture from indirect violence are, however, not unusual. The diagnosis may be difficult without the X-ray, especially when there is much swelling and much tenderness. The points to be observed in diagnosis are crepitus, unnatural mobility, displacement, ecchymosis, and swelling. Mackenzie (*Pract.*, Oct., 1908).

Of 401 cases of injury to the wrist, the writer found the scaphoid broken in 24, the semilunar in 5, the os magnum in 1, the unciform in 2, the trapezoid in 2, and the cuneiform and pisiform each in one. Fracture of the carpal bones a relatively frequent condition. Bendixen (*Internat. Jour. of Med. and Surg.*, July, 1924).

A favorite splint is made by fastening the hand over a soft ball by means of a strip of adhesive plaster. An anterior splint well padded up in the palm serves equally well.

The best method of treating metacarpal fractures is by a long, palmar splint with adhesive strips at the wrist for counterextension and two strips applied to the finger after the manner of Buck's extension apparatus; pads are placed above and below the line of fracture to prevent displacement.

In fracture of a finger, an important point in the treatment is to maintain the alignment of the phalanx, and especially to guard against rotation of the distal fragment upon its long axis. In a compound fracture, the greatest care must be exercised in procuring absolute surgical cleanliness, since infection spells ruin, necrosis, and suppuration involving functional impairment. Any method of fixation giving complete rest to the part will suffice. A thin, wooden splint, narrower than the finger, is generally recommended, but the author prefers a plaster mold, which can be cut to fit any shape, size, or



condition. *Jas. Jefferson* (Penna. *Med. Jour.*, May, 1912).

Phalangeal fractures are usually compound. The hand may be bound over a roller bandage by means of several strips of adhesive plaster, one for each finger. Straight posterior splints may also be used.

The writer encircles the wrist with 8 or 10 turns of plaster bandage extending below the styloid processes, fastens a longitudinal splint to the wrist by a second plaster bandage over the first, and institutes extension with rubber tubing 5 or 6 millimeters in diameter, passed through a loop of adhesive beyond the finger tip, through a hole in the splint. *Lance* (*Presse méd.*, Aug. 8, 1918).

## FRACTURES OF THE PELVIS.

**Fractures of the Ring.**—Under this title are grouped all fractures that dissolve the continuity of the pelvic ring. Such fractures must, of necessity, be vertical in the main. They are usually caused by a crushing from before backward. The line of fracture usually runs through the upper (just internal to the pectineal eminence) and lower (near its junction to the ischium) rami of the pubic bone. Such a fracture may be bilateral, and associated with a vertical fracture of the sacrum, a separation of the sacroiliac synchondrosis, or a fracture through the ilium behind the acetabulum. These are the double vertical fractures of the pelvis. This double fracture may also occur from a fall on the foot, or the same cause may dislocate the os innominatum at both symphyses. Or it may cause a radiating fracture of the acetabulum with or without penetration of the femoral head through the bone. Fractures of the ring are usually comminuted. Displacement of small

fragments or a general mobility, with crepitus, of the whole pelvis may often be recognized. In double vertical fracture the fractured bone is often tilted; so that the superior strait is widened, the inferior strait narrowed, and the limb apparently shortened. Rupture of the membranous or prostatic urethra is almost inevitable, and the other common injuries are rupture of the pelvic vessels, the rectum, the bladder, and the ureters.

**TREATMENT.**—The associated injuries demand immediate attention. For the fracture itself rest in bed with even compression all around the pelvis is all that can be done, except in cases of tilting of the os innominatum, in which traction should be made as after fracture of the thigh.

X-ray and rectal examinations are always indicated in pelvic fractures. *H. C. Mitchell* (*Ill. Med. Jour.*, xxxiii, 107, 1918).

Injury of the urinary apparatus was found only in 2 out of 7 cases of fracture of the pelvis. If the urethra is ruptured, **suprapubic cystostomy**, or at least **puncture**, should be done at once. Clear urine shows that the obstruction is below, and this can await subsidence of the shock. *Guibal* (*Jour. d'urologie médicale et chirurgicale*, Apr., 1923).

**Transverse fracture of the sacrum** results from direct violence. The angular displacement forward may be corrected by pressure from within the bowel. A tendency to recurrence has been prevented by the adaptation of the urethral striated cannula to the rectum.

**Coccygeal fracture** resembles dislocation. It is rarely observed.

**Fractures of the ilium** are comparatively frequent and the result of direct violence. The crest of the

various spinous processes may be broken. The treatment is rest in bed.

**Fracture of the ischium** in any of its parts is rare.

**Fracture of the pubes** not extending across both rami is also infrequently met with.

**Fracture of the Acetabulum.**—Fracture of the rim may complicate dislocation of the hip and may be so extensive as to favor recurrence. Stellate fracture may be indicated by pain on pressure through the thigh. If the head of the femur has perforated the acetabulum it should be replaced by traction.

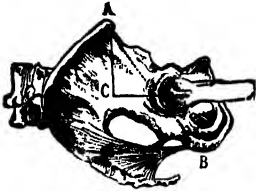


Fig. 7.—A-C-D, Bryant's iliofemoral triangle. A-B, Nelaton's line. (Owen, *American Text-book of Surgery*.)

Report of the case of a boy aged 10½ years who, while descending a stairway, was struck by a heavy falling weight on the right shoulder and thrown to the ground. Sharp pain was felt at once in the inguinal and lower ileocecal regions. The writer was consulted after treatment had been given for 9 days for fracture of the neck of the femur. Examination showed the lower right limb in complete extension but without any tendency to external or internal rotation. The right leg showed a shortening of about 2 cm. as compared with the left. No pain was felt on pressure on the great trochanter along the entire femoral diaphysis to the femoral condyles. Pressure in the right crural region elicited sharp pain in the right suprapubic region, where a distinct swelling was palpated; movements of flexion of the right thigh on the pelvis and of internal and external rotation were

painful but slight extension movements were not. All movements of the thigh were communicated to the tumor mass. The symptoms pointing neither to a fracture of the neck of the femur nor to a luxation of the hip, there remained only 2 possibilities: Either the acetabular cavity had been forced in, or there was total fracture of the acetabulum. The author favored the latter assumption because: (1) in cases of embedding of the acetabulum flexion is either very limited or absent, (2) the characteristic crackling sound on rotation was lacking, and (3) the ease with which the limb could be put in its normal length and position without causing pain. E. Casati (*Policlinico*, xxviii, sez. prat., 118, 1921).

**FRACTURES OF THE FEMUR.**—**Fracture of the Neck of the Femur.**—The division of these fractures into intracapsular and extracapsular has no clinical value and is not borne out by post-mortem findings. The more accurate classification is: (1) fractures through the narrow part of the neck, and (2) fractures at the base of the neck. Clinically, it is often impossible and never necessary to distinguish between the two.

**SYMPTOMS.**—The chief deformity is shortening of the limb with eversion. The eversion is usually slight, often absent, and rarely exchanged for inversion. The shortening may appear at once or may only come on gradually. In the latter case, under appropriate treatment the shortening may never appear at all. In measuring for shortening the greatest care must be taken to compare the limbs when placed in exactly similar positions. There is also a fullness in the outer part of Scarpa's triangle, and the fascia lata above the great trochanter is relaxed, as compared with

the other side, on account of the elevation of the trochanter. Normally the upper border of the great trochanter just touches Nélaton's line drawn from the anterior superior spine of the ilium to the tuberosity of the ischium (*A-B*, Fig. 7). In fracture of the neck, with shortening, the trochanter rises above this line, and the amount of displacement may be measured by means of Bryant's ilio-femoral triangle, variations in the length of the line *C-D* (which is at right angles to *A-C*, a perpendicular dropped from the anterior superior spine of the ilium) indicating the displacement of the trochanter. If the trochanter is split, it is broadened in comparison with its fellow.

Crepitus can rarely be obtained. Pain may be diffuse, but pressure over the neck of the femur is likely to be painful, as is upward pressure of the femur. A few cases are reported in which the patient has walked on the limb, but usually loss of function is complete and all the movements of the joint restricted.

The history of a typical case is as follows: An elderly person, preferably a woman, while walking about, stumbles and falls to the floor, with perhaps little violence. She cannot rise, and complains that every movement of the hip is painful. Examination will reveal symptoms as indicated above.

**DIAGNOSIS.**—The diagnosis between the fractures through the neck and those at the base is often impossible. Splitting of the trochanter is a sure sign of the latter, while after the former it is believed that shortening is more likely to be secondary.

In dislocation the motions of the limb are restricted in certain definite

directions and the head can be felt while in the usual dorsal dislocation; the emptiness of the acetabulum may be determined by pressure on Scarpa's triangle.

In subtrochanteric fractures the trochanter does not share in gentle rotation imparted to the shaft.

In old persons it is not rarely an absolute impossibility to differentiate contusion of the hip from fracture of the neck of the femur. In such a case, when the sole symptoms are pain and disability, treatment for fracture should be instituted without the slightest hesitation, the patient being bedridden in any event, and this treatment should be continued for at least three weeks and until all pain and soreness have disappeared. Thus, if it turns out to be a contused hip, the patient has not been unduly inconvenienced, while if it be a fracture he has been given the best chances of recovery and the surgeon has, perhaps, avoided a suit for malpractice.

**ETIOLOGY.**—As has already been indicated, fracture of the neck of the femur is usually caused by a comparatively slight injury to an old person, usually a woman. In the young a much greater amount of violence is required to break the bone.

**PATHOLOGY.**—In fractures through the neck the cancellous tissue is crushed, but impaction is rare. The head of the bone may be splintered. As a portion of the periosteum habitually remains untorn, the vitality of the head is insured thereby, and union, fibrous at least, may be expected. Fractures at the base are likely to be impacted and the line of fracture may split the great tro-

chanter. The greatest impaction is usually behind; hence the thigh tends to rotate outward. The callus is often excessive.

**PROGNOSIS.**—The prognosis, even as regards life, is far from cheering. The aged and feeble patient is liable to pass into a cachectic or demented

Premonitory signs of dementia must be watched for, and if the patient seems to be failing he must be gotten out of bed, whether his thigh has united or not. In this event the hip should be disturbed as little as possible and the patient allowed to recline in a wheel-chair. Pressure over

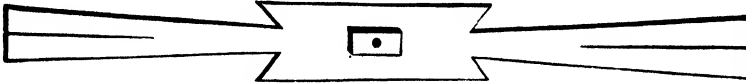


Fig. 8.—Adhesive plaster cut for Buck's extension. (*Stimson.*)



Fig. 9.—Adhesive plaster folded for Buck's extension. (*Stimson.*)

state and thus to fade away, often hypostatic pneumonia.

Or he may die in a few days by the shock. After he has passed the third week, however, the prognosis is good. As to union, it may be fibrous or fail entirely, such a result entailing in some cases no disability to speak of beyond the inconvenience

the trochanter will encourage union, the pressure to be made by a pad under a pelvic band worn as tight as is compatible with the patient's comfort.

From a comparative study of 116 cases of fracture of the neck of the femur, mostly past 60 years of age, the writer believes that the mortality is less in cases properly treated in a

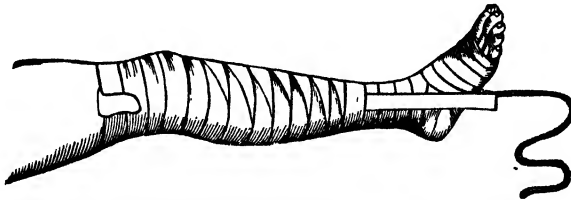


Fig. 10.—Adhesive plaster applied for extension. (*Stimson.*)

of a shortened limb, while in others locomotion may be entirely lost.

**TREATMENT.**—The first indication is to save the patient's life, and to this all else must be subordinate. Such splints should be applied as will most promote the patient's comfort, and the disturbance of repeated measurement and redressing avoided. Careful nursing, feeding, and stimulating are of capital importance.

plaster cast than with any other method. He applies a cast from the nipple line to the toes. The patient's position is changed every 2 hours for the first week and thereafter every 3 hours. Very old or very feeble patients are placed in a special chair and encouraged to eat their meals in this position. Walking on crutches is allowed at the end of 3 months, but weight-bearing is not permitted for at least 6 months. W. C. Campbell (*Annals of Surg.*, lxx, 600, 1919).

In **Buck's extension** the traction is made by weight and pulley over the foot of the bed, which may be raised for counter-extension. It is applied as follows: A strip of stout adhesive plaster (the so-called "moleskin-diachylon" plaster, although it is rather difficult to apply, requiring to be heated before it will adhere—and if overheated it will blister the skin—is least irritating), four inches wide

above it, and the bandage continued up over the plaster (Fig. 10). The cord is then carried over the pulley at the foot of the bed and attached to a weight of from 5 to 20 pounds, the heavier weights only being applied to robust and young patients whose shortening is not done away with by the lighter ones. Outward rotation is prevented by employing Volkmann's sliding rest (Fig. 11),

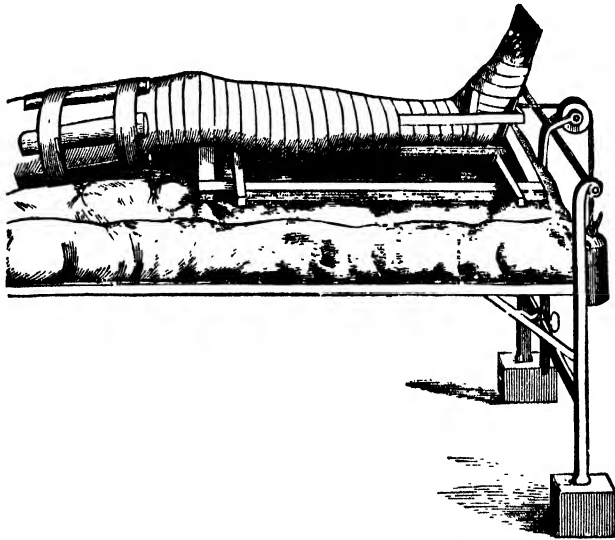


Fig. 11.—Volkmann's sliding rest for fracture of the thigh. (*American Textbook of Surgery.*)

and long enough to reach from well above the knee loosely around the sole of the foot and back above the knee again, is cut as shown in Fig. 8, and a small perforated block of wood placed at its center. Through the hole in the wood and a corresponding one in the plaster a cord is passed, so knotted at the end that it cannot slip through. The edges of the plaster are now turned down over the block and each other (Fig. 9). A roller bandage (preferably of flannel) is applied to the foot and lower third of the leg, the adhesive plaster applied to the sides of the leg and thigh

and sand-bags along the outer side of the thigh.

**Hodgen's splint** (Fig. 12) consists of two iron rods slightly bent at the connection of their upper and middle thirds and attached together by a straight bar at the lower ends and a curved one at the upper. The limb being attired as for Buck's extension (Fig. 10) the cord is attached to the straight cross-bar and a number of narrow compresses or pieces of bandage are pinned to one rod, passed under the limb, and pinned to the other in such a way as to give uniform support to the limb when

it is raised from the bed. The apparatus is supported by two loops tied to a cord which is attached to a crane at a point at least four feet above the bed and at an angle of about ten degrees from the vertical.

**Traction hip-splints**, such as are used in hip-joint disease, have also been applied here. Their use is certainly a great convenience and will

geon need have no hesitancy in separating the fragments. By the abduction or the operative methods of treatment the patient may be saved much disability. For adequate support, the cast should pass from the nipple line to the ankle of the affected side and to the knee of the unaffected side during the first weeks of treatment.

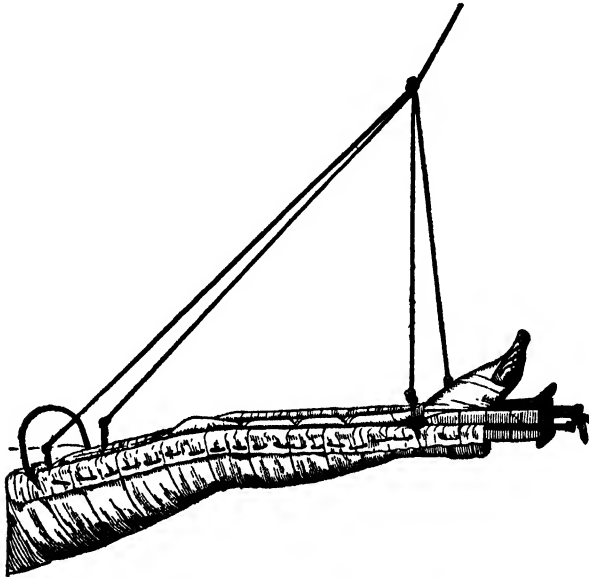


Fig. 12.—Hodgen's splint. (*American Textbook of Surgery.*)

doubtless be more frequent in future. Unfortunately, however, they cannot be used by the very ones who need them most—the aged and infirm.

When the shortening has once been reduced some surgeons prefer to apply a **plaster splint** from waist to ankle at once. Pressure may be made over the trochanter through a fenestra to encourage union.

Of the non-operative methods, **Whitman's treatment** by use of an extensive cast with the thigh held in **marked abduction** has given excellent functional results. With impaction in a poor position, the sur-

In the author's method, the patient, under anesthesia, is placed upon a pelvic support provided with a perineal bar. If the fracture is complete, the trochanter having been lifted to the normal plane, the shortening is reduced by direct manual traction on the extended limb, which is at the same time rotated inward, thus opposing the fragments. Both limbs, extended and under manual traction, are then abducted to the full limit, on the sound side first, to demonstrate the normal range and to balance the pelvis. When this limit is approached on the injured side the tension on the capsule aligns the fragments in a horizontal plane, and finally forces the neck fragment against the inner and

resistant head fragment. This mutual pressure, the first essential of stability, is further assured by the inclusion of the line of fracture within the acetabulum by the apposition of the trochanter and the side of the pelvis, and by the muscular impotence incidental to complete abduction. A long plaster spica is then applied, which, by fixing the limb in complete abduction, extension, and slight inward rotation, insures the continued effectiveness of the anatomical splinting. Out of 28 intracapsular (central) fractures thus treated, 24 recovered with bony union and good function (89.2 per cent.). Similar results were attained in the extracapsular cases. Whitman (N.Y. State Jour. of Med., Dec., 1920).

**OPERATIVE TREATMENT.**—The best treatment of fracture of the neck of the femur without destruction or absorption of the neck is by **operation** with the introduction of an **autogenous bone peg**. That made from the fibula, by reason of its size and strength, is especially desirable. The femur is drilled from the great trochanter, through the neck, into the head of the bone, and the bone transplant firmly driven or screwed into place. Where the neck has been absorbed, as shown by X-ray study in eversion and inversion, **Brackett's operation** is to be preferred.

In fractures of the femur in the aged, the writer recommends **artificial impaction**, which affords immediate bony contact and insures an adequate blood supply for union. With the patient under anesthesia, the limb is placed in extreme abduction and strong traction, with slight internal rotation. The great trochanter, protected by 2 layers of felt, is struck 3 or 4 swinging blows with a large wooden mallet. A light **plaster-of-Paris cast** is applied extending from below the knee to the waist line and including the sound limb to the knee.

The anesthesia lasts only 5 or 10 minutes, and there is no shock to the patient. The latter is placed on a fracture bed equipped with a special frame and elevating device, enabling the nurse to raise him with ease. The cast may be removed as early as the eighth week; but if well borne, it should be left on for 12 weeks. By the end of the fourth month the patient is up and about on crutches. C. D. Lockwood (Trans. West. Surg. Assoc.; Jour. Amer. Med. Assoc., Jan. 10, 1920).

Excision of the head for non-union has been done with varying success.

#### **Fractures of the Great Trochanter.**

—The trochanter alone may be separated by direct violence, or the line of fracture may pass through the neck above the lesser trochanter and thence through the lower part of the great trochanter. In such cases there are the usual signs of fracture of the neck, to which are added independent mobility of the trochanter and a prominent tender spot in front of it.

#### **TREATMENT.—Hodges's splint.**

**Fracture of the Shaft.**—Under this head may be included both "subtrochanteric" and "supracondylar" fractures. The line of fracture is usually oblique and there is both overriding and angular deformity. As the line of fracture usually runs downward and forward the angle is made by the posterior fragments being drawn up behind it. The upper fragment is often rotated outward. In fractures of the upper third the upper fragment is usually abducted. In those of the lower third its sharp point is liable to pierce the quadriceps and even the skin. The shortening may be determined by measurement, the abnormal mobility by gently elevating the limb beneath the point of fracture. The trochanter is not dis-

placed upward. A complicating synovitis of the knee is common, laceration of the great vessels rare.

**PROGNOSIS.**—Shortening of about an inch should be expected.

**TREATMENT.**—Reduction is to be made gently. In fractures of the lower third, if the upper fragment has pierced the quadriceps and cannot be disengaged by traction with the knee and hip strongly flexed, reduction must be made through a free incision.

Immobilization can be secured with **Hodgen's splint**, but is best made by the **Thomas traction splint**. For general use, the Thomas splint is unexcelled, having produced in the world war, in fractures of the femur, results far superior to those obtained in civil practice. It provides immobilization with access in case of compound fracture. It is important that the foot be kept at a right angle, that the normal anterior curve of the femur be supported, and that sufficient traction be used to produce complete reduction, or better slight elongation, on the affected side. To increase the extension, traction may be made to the splint from a **Balkan frame** or other piece of apparatus attached to the patient's bed. Traction should be maintained for about eight weeks, and support, as by a **plaster cast or caliper splint or brace**, continued for four to six months, especially where operative treatment has been used. Many cases in which the bone has been plated have failed from lack of external support for a sufficiently long period of time.

The *position of fixation* for injuries of the shaft of the femur without flexion or abduction of the upper fragment should be 10° flexion and

abduction at the hip and anterior superior spine, the mid-point of the patella and the space between the second and third toes being in the same straight line. The foot should be dorsally flexed to a right angle.

Analyzing the results in fractures of the femoral diaphysis in children under 12 years of age, the writer warns that operations for fresh fractures of the femoral shaft in children are to be avoided. Immediate treatment should be given; every hour of delay diminishes the ease and possibility of perfect reduction. Plaster casts are inadequate to maintain extension and alignment. The most efficient method of holding the reduction is **continuous suspension traction** by means of a suspension splint and overhead frame. Walking should not be allowed until a walking caliper splint is fitted to the patient. This allows his weight to be borne on the ischium, and should be worn for 3 to 6 months after he gets up or until the callus has become sufficiently hardened for weight-bearing. In most cases reduction was effected under anesthesia on a fracture table by mechanical traction. If complete reduction cannot be obtained the surgeon must be satisfied with the best reduction possible, provided it will result in good function, or he must perform an open operation. Lane plates are suitable only for transverse fractures. In late cases all callus must be removed and at 6 weeks the plate should be removed. **Autogenous intramedullary bone pegs** are excellent for patients over 7 years old. K. Speed (Surg., Gynec. and Obstet xxxii, 527, 1921).

When the traction does not correct the deformity in ten days, open operation with reduction should be done.

Ambulatory treatment as for fractures of the neck of the femur has proved satisfactory. Children under 10 are best treated by **vertical sus-**



**pension** of both legs. The pelvis should be elevated about two finger-breadths above the bed, thus making counterextension.

For compound fractures the **double inclined plane** (Fig. 13) is often most convenient. It affords no traction,

Intercondyloid fracture presents the same features as intercondyloid fracture of the humerus.

**TREATMENT.**—Any fracture of the femur involving the knee-joint should be immobilized in extension. A molded posterior splint and slight

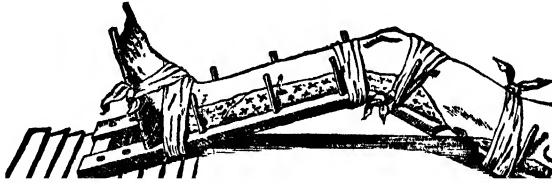


Fig. 13.—Esmarch's double inclined plane. (*Esmarch and Kowalzig.*)

but the loss of bone substance by comminution usually renders traction unnecessary. In other cases Smith's anterior splint, which acts like a suspended double inclined plane, is more appropriate.

**Fractures of the Lower End of the Femur.**—Epiphysiolysis is more fre-

traction will usually prove satisfactory as far as the fracture is concerned; but the chief dangers are gangrene from injury to the popliteal vessels, and ankylosis or suppuration in the knee-joint. Some subsequent stiffness in the knee is always to be anticipated.

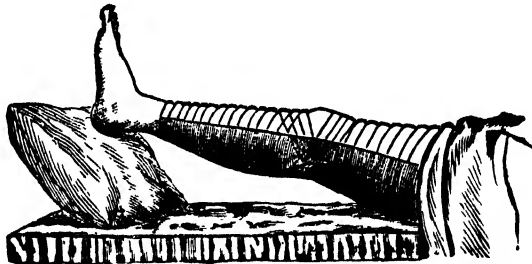


Fig. 14.—Hamilton's dressing for fracture of the patella. The final turns of the roller in front of the knee are not shown in cut. (*American Textbook of Surgery.*)

quent here than at any other point. It occurs as late as the twentieth year, usually from torsion or hyper-extension of the leg. Associated injury to the vessels is common. The treatment is the same as for fractures of the shaft.

Fracture of one condyle is usually due to direct violence. Immobilization should be made with the knee extended.

**Fracture of the Patella.**—This is common between the ages of 20 and 50. It may be comminuted when due to direct violence. Rarely it is vertical. Ordinarily it is transverse and due to muscular action, as in jumping or avoiding a fall. The sudden pull of the quadriceps snaps the bone. The snap and a sharp pain are felt by the patient, and extension of the leg is almost completely lost.

The gap between the fragments is readily palpable, but is usually small at first, for the lateral ligamentous attachments of the upper fragment prevent the quadriceps from drawing it up the thigh. The joint becomes distended with effused blood. The periosteum over the patella is torn irregularly and a fringe of it drops between the fragments.

**PROGNOSIS.**—In the absence of treatment or from its inefficient application the two fragments will be drawn farther apart by the retraction of both the ligamentum patellæ and the quadriceps. Adhesions from organized blood-clot and lacerated ligaments immobilize the joint more or less completely, and extension is still farther impaired by adhesions between the upper fragment and the femur and by the loss of coaptation between the patella and the condyles.

**TREATMENT.**—Non-operative treatment consists in causing the absorption of the fluid in the joint by pressure (massage is of little service) and then immobilizing the fragments until union has taken place. It is advised only for comminuted fractures, those produced by direct violence without rupture of the patellar ligament. A Martin bandage should be applied with as much pressure as the patient can bear for four to six days, and may be continued for a fortnight if it holds the fragments in good position. During this time the patient is kept in bed with the knee extended. A posterior molded splint is then applied from the ankle to near the hip and is bandaged in place as shown in Fig. 14, the turns of the bandage about the knee pressing the tissues above and below the fragments toward each other—these

may be reinforced by strips of adhesive plaster—and finally a few turns are taken over the fracture to prevent tilting forward of the fragments. The dressing must be worn for a month and frequently inspected and altered if necessary. At the end of this time an immobilizing plaster bandage is applied, and the patient allowed to go about on crutches. This splint must be worn for a month, not that union will become much firmer, but so as to accustom the patient to walking about, and to loosen the adhesions a little, that the bone may not be refractured by another fall or slip. During this time **massage** may prove useful, and to that end the splint may be split anteriorly, removed daily, the limb massaged, and the splint replaced and held firmly by a roller bandage. At the end of the second month the patient is discharged, but advised to walk with care. Various splints have been devised to secure immobilization of the knee and coaptation of the fragments, but they present no advantages over the above method. All fail to remove the fibrous tissue almost invariably covering the fractured ends in transverse fracture. A plaster bandage should never be applied until union has taken place. Malgaigne's hooks and their various modifications have had great vogue. The principle involved is the holding of the fragments in apposition by means of sharp hooks, which may be inserted into the upper and lower edges of the bone and drawn together by a screw. The danger in their use is that suppuration, provoked at the points of puncture, may travel into the joint either through the lymphatics or the cellular planes.

especially if there is much effusion of blood. Finally, aspiration has been used—with strictest asepsis—to empty the joint more rapidly than is possible by pressure.

The writer agrees with Schulze in grouping these fractures into those of the patella alone and those with rupture of the collateral ligaments. There are 3 methods of treatment: (1) conservative; (2) subcutaneous or percutaneous suture; (3) open suture. The first is indicated only in the rather unusual fractures due to direct violence in which the power of extension is not destroyed and there can never be separation of the fragments. If there is dislocation of the fragments and more or less injury of the collateral ligaments, operative treatment is indicated, as otherwise there is apt to be failure of union. Moreover, re-fracture is often necessary after conservative treatment on account of connective-tissue union of the fragments.

Of the open methods of operation the authors prefers **peri- and prepatellar suture**. Suture of the bone alone without suture of the collateral ligaments is not sufficient, but following bone suture combined with suture of the collateral ligaments there are apt to be disturbances due to the wire sutures. In compound fractures the writer waits for cicatrization of the external wound and then does a secondary suture. He advises against plastic operations, especially in simple fractures. *Active and passive movements* should be begun 2 weeks after operation. After 3 weeks the patient gets up, and in the third or fourth week *mechanical treatment* is begun. F. von der Huetten (Beitr. z. klin. Chir., cxxi, 687, 1921).

Description of the **pin method** for approximating patella fragments. Strong pins are passed through the tendons very close to the patella, and are then approximated by means of bandages or adhesive strips. This brings the broken fragments in close approximation. The advantage of the procedure is that the bones can

be certainly approximated without entering the knee-joint. Hertzler (Surg., Gynec. and Obstet., Mar., 1921).

Operative measures include various sutures—mediate, immediate, subcutaneous—the trimming off of the fringe interposed between the fragments, and washing out the joint. The following operation is preferred—if operative treatment is elected: Through a median incision extending a little above and below the fragments, sharp hooks are inserted into each fragment, drawing them apart, and the joint is flushed with sterile “normal” salt. The whole line of fracture is now exposed by lateral retraction of the flaps, and, *without touching the tissues with his fingers*, the surgeon elevates any interposed fascia and periosteum and holds them and the fragments in place with a few fine catgut sutures. A suture or two may also be taken in the capsule of the joint, if it is widely torn. The torn lateral expansions of the patellar ligament are carefully sutured after clearing the bone ends. Wiring or suturing the bone is unnecessary. The skin is then sutured with silk. No drainage. A plaster bandage is applied and the patient sent to bed, where he remains with his foot elevated for a week. The splint is then removed, the skin sutures taken out, and the splint reapplied. A few days later the patient gets up on crutches. These and the splints he wears for a month. The splint is then cut down again, and he wears it in the daytime alone for another month. No further treatment is required. The operation may be done under **cocaine**. The reason for giving preference to this operation over any other

is that it fulfills the indications of washing out the joint, complete reduction, and firm immobilization in a thoroughly aseptic manner, and leaves behind no foreign body in the joint to set up suppuration or irritation. By keeping his hands from contact with the tissues the surgeon makes the operation as safe as, and safer than, any subcutaneous one, as has been borne out by the experience of 90 consecutive cases without suppuration (Stimson).

*The Choice of Treatment.*—The results of immobilization vary from a perfect functional result with about one-fourth inch separation to absolute loss of function with wide separation or stiffness in the joint. Such results are attained within about six months. Operation may give a perfect result with linear union, but, on the other hand, postoperative suppuration in the knee-joint may prove fatal. If the operation is successful the patient saves about two months of convalescence and a great many of the doubts and annoyances incident to mechanical treatment. Therefore the operation is to be preferred, if the risks of suppuration can be absolutely eliminated. Such is the case only when the surgeon is sure of his own cleanliness, as well as that of his assistants and instruments, is conversant with operative and aseptic technique, and is sure to keep his hands out of the wound. Under such conditions operation is to be elected, with the patient's concurrence.

If function is impaired by failure of union, operation is the only resource. For lengthening the contracted quadriceps its tendon may be nicked at the more tense places, and its lower fibers may be elevated from the femur.

Care must be taken, however, not to impair the vitality of the tendon and the fragment of the patella attached to it.

### FRACTURES OF THE LEG.—

**Upper End.**—Both bones may be fractured, or else the tibia alone. The avulsion of the spine of the tibia by the crucial ligaments is merely a complication of dislocation. A few cases of epiphysiolysis and longitudinal fracture of the tibia have been noted. If the line of fracture runs into the joint its functions may be impaired, and a tendency to displacement with a resultant genu varum or valgum must be foreseen and prevented by immobilization. Permanent traction may be necessary when there is much comminution.

All wounds and fractures of the leg repair far more quickly if the limb is suspended. The **Hodgen splint** bent to an angle of  $135^{\circ}$  is used. Fractures of the fibula are suspended because of the improvement in circulation and for the dressing of wounds, but no traction is necessary. Fractures of the tibia alone are splinted by the fibula, but incurvation is common. A slight traction of one or two kilos will correct this. In fracture of both bones traction of three or four kilos is necessary. Fractures of the tarsus and metatarsus are also commonly treated by suspension. Blake and Bulkley (*Surg., Gynec. and Obstet.*, Mar., 1918).

Avulsion of the tubercle of the tibia is caused by muscular action quite as is fracture of the patella. Recovery of function may be expected if the leg is immobilized in extension on the posterior molded splint and the fragment retained in place by adhesive plaster.

**Shaft.**—The usual seat of fracture is at the junction of the middle and lower thirds, the fibula being fractured

higher than the tibia. The tibia lies so near the surface of the limb that a diagnosis of its fractures is usually to be made by palpation. This subcutaneous situation also serves to make compound fractures frequent. If the tibia is fractured an accurate diagnosis of fracture of the fibula, often very difficult without the aid of the fluoroscope, need not be made. Fracture of the fibula alone may be made out by a localized point of tenderness elicited by direct pressure or pressure elsewhere along the shaft.

Edema and neuralgia are exceptionally apt to complicate convalescence from fractures of this region.

**TREATMENT.**—Reduction is accomplished by traction with the knee flexed to relax the gastrocnemius. A simple method of treatment is to keep the limb in a Volkmann splint until the primary swelling has disappeared, when a plaster bandage is applied from the toes to the knee, and changed every ten days until union takes place—the sixth week.

Should bony union be delayed, the irritation of bearing some weight on the limb in its plaster incasement may prove beneficial. From the time of the application of the plaster splint the patient gets about on crutches. If it is wished to have him about from the first the Volkmann splint may be replaced by a twin posterior molded splint, the two halves of which, when they reach the ankle, diverge to cross each other on the dorsum of the foot.

The subject of ambulatory treatment has already been dealt with in the section on general treatment.

Compound fractures are best dressed through a Volkmann or fenestrated plaster splint.

**Lower End.**—Fracture of the shafts of both bones low down, and irregular comminuted fractures require immobilization with the foot at right angle to the leg. Primary amputation is indicated for badly comminuted compound fractures. The common fractures here are fractures by eversion and abduction (Pott's) and fractures by inversion (external malleolus and rarely the internal one).

The *position of fixation* for fractures of the tibia and fibula should be with the knee slightly flexed, the foot dorsally flexed to a right angle, and the midpoint of the patella and space between the second and third toes in the same straight line.

The writer reports good results in 16 cases of oblique fracture of the tibia by driving in a long nail, slanting, to hold the fragments. The nail was removed in from 5 to 23 days. The results were perfect in 11 cases reexamined from 3 to 6 years later except in 5 cases in which the limb was shorter by 1 to 3 cm., the latter in a man of 61 with comminuted fracture of both bones. P. F. Nigst (Schweizer med. Woch., Jan. 27, 1921).

**Pott's Fracture.**—This is the commonest fracture of this region. It is caused by eversion and abduction of the foot. There is a typical displacement of the foot outward and backward. Lateral mobility in the ankle-joint, combined with points of tenderness over the internal malleolus as well as the tibiofibular articulation in front and over the fibula above the malleolus, are pathognomonic signs of this fracture. These tender points lie over the three typical lines of fracture, as shown diagrammatically in Fig. 15. The posterior portion of the articular surface of the tibia may also be crushed. Rupture of the deltoid

## FRACTURES (STIMSON AND BABCOCK).

and tibiofibular ligaments may replace the tibial fractures. The typical deformity is caused by the loss of the normal support to the inner side of the foot, and tibiofibular diastasis, which allows the astragalus to slip backward, sometimes so far that it may be quite behind the tibia. If the displacement is not great the patient can walk, though painfully. The fracture of the internal malleolus may be compound.

**TREATMENT.**—To effect reduction the foot must be forced forward and inward, and immobilized in inversion. To maintain reduction posterior and



Fig. 15.—Usual three lines of fracture in Pott's fracture at ankle. (Stimson.)

internal plaster-of-Paris splints are very serviceable, the former to extend from the upper third of the leg to the toes, the latter from the same level down to and around the foot, ending at the outer side of the dorsum, the so-called "stirrup-splint." In uncomplicated cases the patient may be allowed to get about on crutches as soon as the primary swelling has abated—a new splint being then necessary—and after that need only be seen often enough to forestall any recurrence of the deformity. It is in Pott's fracture that ambulatory splints are most likely to be of practical use. Some patients can walk with only the support of a shoe, for,

as we have seen, the deformity is angular, outward, and backward, and as long as this angular deformity is prevented the functions of the limb are but little impaired. A plaster incasement fortified on the outer side and behind may meet the indications very satisfactorily. It should extend from the toes almost to the knee and



Fig. 16.—Pott's fracture. Dupuytren's splint. (Scudder.)

be firm and heavy. The Dupuytren splint is sometimes used (Fig. 16).

If the fragment of the internal malleolus cannot be reduced the knife must be resorted to.

While the results that follow careful treatment are perfectly satisfactory, old reduced fractures are very troublesome. They may be improved and sometimes cured by supramalleo-

an osteotomy, or, better, by opening both sides of the joint, chiseling through the old lines of fracture, removing obstructing callus, and reducing the fracture as though it were a recent one.

**Fracture of the External Malleolus.**—This occurs by the opposite force from that which produces Pott's fracture, namely: inversion of the foot. If, as is usually the case, the fibula alone is broken, or the fibula and the tip of the internal malleolus are broken, it is sufficient to immobilize the foot while it is pressed well inward to prevent widening of the mortise. But if the lower end of the tibia is broken obliquely across, as sometimes occurs, special attention should be paid to the backward displacement.

Attention called by the writer to a type of ankle fracture featured by a fracture of both malleoli with a splitting away of a wedge, large or small, from the back surface of the tibia at the joint, with dislocation up and back of the foot. Sometimes the internal malleolus is included with the tibial segment in 1 piece. The fracture of both malleoli frequently causes confusion with Pott's fracture. The writer has seen 53 of these fractures in 7 years. In fresh cases he reduces the dislocation by forward traction with the muscles relaxed in moderate plantar flexion; after reduction, plaster is applied with the foot in maximum dorsal flexion. In old cases he operates, incising on the outer and inner sides, dividing both malleoli above the joint, loosening up the whole joint and, if necessary cutting out a fresh joint surface on the forepart of the tibia for the astragalus. F. J. Cotton (Jour. Amer. Med. Assoc., Jan. 23, 1915).

## FRACTURES OF THE FOOT.

—**Fractures of the Astragalus.**—This is usually associated with fracture of

the os calcis, being caused by a fall on the foot. If there is no displacement the skiagraph is required for diagnosis, and the only treatment is immobilization of the foot. If, however, a fragment is displaced and cannot be reduced, or if the bone is crushed, the fragments had best all be removed, a complete excision of the bone giving very good results.

**Fractures of the Calcaneum.**—This may occur from direct violence, from strain on the plantar ligaments, and from forcible action of the muscles of the calf, putting the tendo Achillis on the stretch. Three weeks are required for solid union. If the fracture separates the sustentaculum tali, the limb must be immobilized with both knee and ankle flexed.

**Metatarsal Fractures.**—Rest, elevation, and massage will suffice for the cure of single fractures. Multiple fractures require a splint.

LEWIS A. STIMSON,  
New York,

AND  
W. WAYNE BABCOCK,  
Philadelphia.

## FRAMBESIA. See YAWS.

**FREEZING.**—Freezing may affect the entire body; or, only a part of the body may be involved, as instanced by *frost-bite*. There are three degrees of frost-bite: (1) erythema, or redness; (2) blistering; (3) gangrene. A chilblain is a frost-bite of the first degree where the redness clears up in a few days, but reappears again upon exposure. Chilblain is treated under PERNIO.

**SYMPTOMS OF FREEZING OF BODY.**—Cold is primarily a stimulant, secondarily a depressant to the body cells. After prolonged exposure, drowsiness and numbness are experienced. The body is pale, the blood being driven to the internal organs, which become markedly congested. Finally, the individual falls into a deep sleep, the pupils become dilated, the pulse

slow, the respirations slow and stertorous. The body is cold and finally death occurs.

#### **SYMPTOMS OF FROST-BITES.**

Freezing first causes a numbness of the parts, followed later by an anesthesia. There is a feeling of weight, coldness, extreme pallor, and, early, a sense of prickling or tingling. If the cold is very intense and applied suddenly the parts may have a mottled appearance. When the parts are warmed, there is extreme itching and burning of the parts, together with redness and swelling.

There is great swelling and lividity of the parts in frost-bites of the second degree, followed later by the formation of blisters. Often ulceration or gangrene follows. An ulcer due to this cause is usually superficial, but is difficult to heal. The necrotic tissues are moist and the seat of a thin, ichorous discharge. The surrounding tissues are usually quite inflamed. In frost-bites of the third degree the part is pale and insensitive. There is sometimes excruciating pain in the parts above. The part is cold, edematous, and swollen, but later becomes discolored and shrivelled and a line of demarcation forms. (See **GANGRENE**, next page.)

**TREATMENT OF FREEZING OF ENTIRE BODY.**—The patient should first be taken into a cold room and gentle friction with cold cloths used. The temperature of the room should be gradually raised as the circulation and respiration return to normal. The friction should be gradually increased and brandy or spirit of camphor may be used. Later brandy may be given by mouth or by rectum, the patient covered lightly and the extremities

elevated. **Artificial respiration** should be used if needed. Warm broths and warm drinks should be given as the patient recovers.

#### **TREATMENT OF FROST-BITES.**

In frost-bites of the first degree the parts should be rubbed with ice-water or snow. Warmth to the parts is more efficient, according to some, but the sudden use of heat is harmful.

Heat applied too rapidly in frost-bite causes gangrene. A moist gangrene should be converted to dry gangrene by removal of the epidermis and the application of dusting powders, such as bismuth subgallate, airol, and animal charcoal. Amputation should be delayed until a line of demarcation appears. X-ray treatment for moist gangrene and tetanus antitoxin for prophylactic purposes have been urged. Flörcken (Therap. Halbmonatsh., July 15, 1921).

As the circulation returns to normal the temperature of the room should gradually be raised, and the parts rubbed either with the hand or with a warm solution. In frost-bites of the second degree, especially with marked inflammatory reaction, free incisions should be made. Silver nitrate or tincture of iodine may be painted on the part. Ulcers should be treated antiseptically, the same measures being used as in ulcers due to any other cause.

During the war paraffin applied as for burns proved useful; also Bier's hyperemia. Camescasse (1918) found picric acid 0.25 Gm. (4 grains), alcohol and glycerin, of each, 10 Gm. (2½ drams), painted on and allowed to dry, very helpful.

## **G**

**GALLIC ACID.**—Gallic acid occurs as fine, needle-like crystals, whitish in color, odorless, and having an astringent, slightly acid taste. It is soluble in about 100 parts of water, 5 parts of alcohol and 40 parts of ether. It is incompatible with all the ferric salts, ammonia, silver salts, lead acetate, and potassium chlorate.

#### **PREPARATIONS AND DOSES.**

*Acidum gallicum* (gallic acid) is given in

the dose of from 5 to 20 grains (0.3 to 1.3 Gm.) It is no longer official.

The ointment of gallic acid (*unguentum acidi gallici*) is used for local applications.

**PHYSIOLOGICAL ACTION.**—Gallic acid acts as an antiseptic, astringent and hemostatic, and is eliminated by the kidneys. It is also mildly antiseptic.

**THERAPEUTICS.**—Gallic acid may be used externally in epistaxis; hemorrhoids;



certain skin diseases, especially **psoriasis** and **alopecia**, and may be applied locally to **ulcers** which are actively discharging. Internally, it has been used in **night-sweats**, in **intestinal hemorrhage**, and in **diarrhea** due to atony of the intestinal glands.

**GAMBIR.**—Gambir (or *pale catechu*) is an extract from the leaves of *Ourouparia gambir*. It has a grayish- to reddish-brown color, a bitterish, very astringent taste, and is insoluble in water. It is incompatible with the iron compounds, mercury bichloride, zinc sulphate, and lime water.

**PREPARATIONS AND DOSES.**—*Gambir*, U. S. P. (*gambir*). Dose, 15 grains (1 Gm.).

*Tinctura gambir composita*, U. S. P. (compound tincture of gambir), representing 5 per cent. of gambir and 2.5 per cent. of cinnamon. Dose, 1 fluidram (4 c.c.).

**PHYSIOLOGICAL ACTION AND THERAPEUTICS.**—Gambir is an astringent and a hemostatic, considerably used as a component of mouth-washes in conditions in which **spongy gums** are present. Lozenges of gambir, each containing 1 grain (0.06 Gm.), have been deemed of service in throat disorders, especially **acute** and **chronic pharyngitis** and **mild laryngitis**. Internally, the drug has been used in **gonorrhea**, **leucorrhea**, and **diarrhea**, especially in the serous type of the latter disorder.

**GANGOSA**, also termed "rhino-pharyngitis mutilans," is an ulcerative disease of the upper respiratory tract, including, in some instances, the osseous tissues. It is observed in various tropical countries, particularly in Guam and several other islands of the Mariana group, the Ladrone and Caroline islands. It is sufficiently contagious to have caused Spanish authorities of Guam to segregate the patients, a precaution which, discontinued after the American occupation, has increased the prevalence of the disease.

Its etiology is still obscure, but flies and other insects have been deemed the main agents of transmission, through an organism which resembles the *Bacillus diptheria*, but specific as to the nature of the lesions caused. These are wart-like tubercles or nodules which may involve the skin,

mucosa, and rarely the bones of the upper respiratory tract and lips. It is by many believed to be rhinoscleroma.

According to A. Breinl (*Annals of Trop. Med. and Parasit.*, June, 1915) it is due to small bodies resembling yeast cells which he found in the edema fluid of several cases. He believed that these cellular parasites belong to the genus *Cryptococcus* of the family *Saccharomycetes*. He terms the organism *Cryptococcus mutilans*.

**Treatment.**—Early antiseptic treatment limits the extension of the disease. **Iodine**, **phenol**, **nitrate of silver** and **chromic acid** are used to destroy the infected area, with a weak solution of **potassium permanganate** as deodorant. Internally, **potassium iodide**, 5 grains (0.33 Gm.) three times a day, has been found effective—a fact which speaks in favor of the parasitic theory.

Case of gangosa in a Borneo woman. The process was promptly arrested by **neoarsphenamin**, but left a large hole by the destruction of the nose. Waar (*Nederl. Tijdsch. v. Geneesk.*, Mar. 21, 1925).

### GANGRENE.—DEFINITION.—

This term is usually applied to death or mortification of soft tissues, while the term "necrosis" is reserved for death of osseous or cartilaginous tissues.

**VARIETIES.**—Gangrene is divisible into several varieties: *Moist gangrene*, due to arrest of the vascular supply, and in which the parts are soft and pulpy; *dry*, or *senile gangrene*, or mummification, occurring in old age, in which the tissues become leather-like and wrinkled; *spontaneous gangrene*, a relatively rare form affecting the extremities and observed in apparently strong and young subjects; *ergot gangrene*, which occurs in individuals who, in consuming rye or rye bread, become exposed to ergot of rye; *diabetic gangrene*, which occurs as a complication of advanced diabetes; *pressure gangrene*, due to pressure and which occurs occasionally as a complication of bed-sores; and *symmetrical gangrene*, or Raynaud's disease, a paroxysmal form affecting mainly the tips of the fingers and toes.

**SYMPTOMS.**—The symptoms vary greatly according to the primary pathogenic factor and, to a degree, with the location of the gangrenous process.

**MOIST GANGRENE.**—This variety is that most frequently met, owing to its frequent occurrence as a result of accidents, irreducible hernia, etc. Being due to arrest of the blood, both in the arteries and veins, there is softening, or liquefaction. The tissues assume various shades, varying from bluish green, red, to black; and blebs containing a very foul and fetid liquid are formed, the mortifying tissues giving off gases composed mainly of sulphide of hydrogen, ammonia, and volatile fatty acids. This form is likely to occur after severe injuries, such as crushing, burning, or even frost-bite. It is also observed when open wounds have been exposed to infection through imperfect or uncleanly dressings. A form of moist gangrene, also of traumatic origin, is sometimes witnessed after a large vascular trunk has been destroyed, which may spread with great rapidity.

In an average case the gangrenous area undergoes, as stated, a characteristic change of color. At first the boundary line between the dead tissues and the living ones is imperfectly marked. Where the progress of the necrotic process is arrested, however, through the vital resistance of the tissues, an area of inflammation interposes itself as a protecting wall, which becomes more or less perfect as the granulation tissue formed is healthy. This constitutes the *line of demarcation*. The inflammatory process continuing beyond, suppuration ensues, and the dead tissues may thus be entirely separated from the living ones through nature's efforts. The inflamed area is distinguishable from the healthy or gangrenous ones by its bright-red color, which changes to blue or black in the direction of the dead tissues. Unfortunately nature's efforts do not always succeed, and the morbid process may penetrate the limiting barrier and invade the tissues beyond, extending gradually until death ensues.

The constitutional symptoms depend upon the amount of tissue involved. At first, when an extremity is affected, there may be but slight general disturbance; when, however, the gangrene ascends the limb, fever and other evidences of toxemia appear.

The extension of gangrene depends to a great degree upon the nature of the cause and the general health of the patient. An injury, which, through interruption of the circula-

tion, is followed by gangrene, often remains circumscribed to the region in which the blood-flow has been reduced or arrested, provided, however, the general condition of the patient is favorable. Persons in poor health, or individuals who have lowered their vital powers by the excessive use of alcohol, overwork, insufficient food, etc., however, are much more exposed to extension of the gangrenous process.

Complications incident upon the destructive nature of gangrene usually lie behind a fatal issue, when this occurs. An artery may be eroded, giving rise to mortal hemorrhage; pyemia and septicemia through penetration into the blood of one of the various pyogenic organisms, peritonitis through extension of the gangrenous process from a gangrenous hernia, etc., may be mentioned among the many death-producing conditions which can appear.

Where gangrene spreads with rapidity, the so-called *traumatic gangrene*, the blood-supply is interrupted and there is septic infection. The gangrene may soon spread up an entire extremity. The skin becomes brownish-red, black, or green; gas is rapidly formed, and the patient quickly succumbs to acute septicemia, unless amputation has promptly relieved him of the source of infection.

In truth, gangrene seldom occurs nowadays owing to modern methods, and, even in severe injuries, separation of the dead tissues soon occurs. Strict antisepsis greatly limits the likelihood of gangrene.

Rigidity in the muscles after an injury of the limb is a warning of impending gangrene to which the writer calls attention. Fievez reported several cases in which hardness of the leg below traumatic injury persisted until gangrene developed. It is evidently a sign of ischemia due to vascular injury. Prat (*Paris méd.*, Mar. 31, 1917).

**DRY GANGRENE.**—In this variety of gangrene, of which senile gangrene is a type, there is a distinct absence of fluids, and the process of mortification is more a metamorphosis into an inorganic mass than a true decomposition; hence the term "mummification" frequently applied to this form. The local blood-supply gradually diminishes, the tissues shrink, become dark brown or black, wrinkled, and the skin be-

comes leathery. It usually affects the toes, sometimes the fingers, and may spread to the plantar or palmar surfaces.

**SPONTANEOUS GANGRENE** is rarely observed. It may be met with in subjects who apparently are in excellent health, but affected, as autopsies have shown, by arteriosclerosis. The arteries are narrowed, and thrombi are sometimes widely disseminated through the affected extremity. This renders spontaneous gangrene particularly malignant, and amputation of the limb is often necessary, preferably above the knee-joint when the morbid process affects a leg. Unlike other varieties, it gives rise to acute suffering, owing to involvement of the local nervous supply, the principal branches of which are often found greatly thickened. Spontaneous resolution is rarely observed in this form. Wormser observed 15 cases of gangrene of the legs in the puerperium.

In the literature the writers found 73 cases which they consider undoubted examples of spontaneous gangrene; 69 patients were males and 4 females; 2 patients were under 20 years old, 7 were between 20 and 30; 9 between 31 and 35; 22 between 36 and 40; 12 between 41 and 45; 10 between 46 and 50; 10 between 50 and 60; 1, age not mentioned. Although the symptoms in 1 case were present for over twenty years, the average duration was from three to five years. In the 68 cases in which the location was mentioned, the condition occurred 53 times in the legs alone, twice in the arms alone, and 13 times in both upper and lower extremities. In more than one-third of the cases the pulse in the femoral and all the vessels distal to it was lessened or obliterated, while in nearly two-thirds the vessels as high as the popliteal were involved. Neither syphilis nor the use of tobacco seemed to play any part in the causation of this condition. The authors report 1 case seen by them. They believe that it was a case of general arterial thrombosis, exactly similar to that found in the extremities in the condition known as spontaneous gangrene.

Dexter and Ellis (Cleveland Med. Jour., Aug., 1910).

A form of spontaneous gangrene simulating purpura, due to an *acute thromboarteritis*, probably of streptococcic origin, is described by the writer. Usually the extremities, upper and lower, are affected. Death may occur in a few days or gradual recovery take place after sloughing of the gangrenous areas. D. W. Kramer (N. Y. Med. Jour., Oct. 4, 1922).

**ERGOT GANGRENE** is also partly of neurotic origin, the main pathological factor being vasomotor spasm brought on by the ingestion of ergot of rye when rye flour is used instead of wheat flour in making bread, as is the case in many parts of Europe. The continued consumption of ergot of rye gives rise to various preliminary symptoms: general adynamia, gastric disorders, formication, and fugitive pains. The arrest of the blood-current through the spasmodically contracted arteries is soon followed by blanching and lowered nutrition, which makes the part vulnerable to the least traumatism. Even without such, the ill-nourished areas farthest from the center—the toes, the ears, the nose, etc.—finally succumb.

**DIABETIC GANGRENE.**—Gangrene is rather frequently observed in diabetics, especially in persons advanced in years. (See also the article on DIABETES, this volume.) Heidenhain attributes it to the common cause of senile gangrene, arteriosclerosis; the main factor he believes to be an abnormal susceptibility to wound infection. Still, the fact that internal viscera sometimes become gangrenous in such cases would tend to invalidate this view. In a case witnessed by Turner the pyramids of the left kidneys were found gangrenous. A marked line of separation existed, and every other portion of the organ was healthy, as was also the entire urinary system.

Hyperglycemia is not a very important factor in the induction of the gangrene, but looms into importance after gangrene has been established in so far that it invites septic infection and encourages the occurrence of the three acid bodies occurring in diabetes. Acetone has a very low degree of toxicity, and probably does

not contribute to the production of gangrene. Diacetic acid is always to be looked upon as a pathological agent, though of itself not very harmful and indicates that betaoxybutyric acid is being oxidized. Betaoxybutyric acid, when present in the urine, is to be viewed as the special chemical agent fostering gangrene, which, however, is ineffectual in bringing about that result if acting alone in the absence of arteriocapillary sclerosis. The quantitative ammonia excretion is the expression of measure of the amount of unburned betaoxybutyric acid. It is not an accurate standard of measurement, always registering too little. The excretion of 1 Gm. in twenty-four hours is to be looked upon as contraindicating operation except in great emergency. Eising (Med. Rec., Aug. 15, 1908).

**PRESSURE GANGRENE.**—This occurs when a region in a low state of vitality—such as occurs in prolonged fevers, etc.—is submitted to continued pressure. The vascular supply, already weakened, becomes further weakened, especially when, as is the case over the sacrum, the scapula, etc., the soft tissues are pinched, as it were, between a bone and the bed. The slightest injury over such a site becomes the seat of ulceration, the so-called “bed-sores,” and gangrene is apt to follow, if through the presence of arteriosclerosis and old age the lumen of the vessels is already limited.

**SYMMETRICAL GANGRENE**, or Raynaud's disease, is a form which occurs in paroxysms. It begins with paresthesia and sharp pains. The tips of the fingers and toes, the parts most frequently affected, then become cyanotic and gangrenous. The entire phalanx is occasionally involved. It is occasionally observed in other parts of the body, the unaffected surfaces being usually very pale.

Case of symmetrical gangrene following local asphyxia in the tips of both ears. This localization is regarded as rare, from the fact that Raynaud, in his description of the condition which bears his name, makes no mention of such lesions occurring about the face save in one instance in which small cicatrices were seen by him about the

nose. In the author's case, anemia seemed to be the main underlying cause. Canessa (Revista medica del Uruguay, vi, No. 4, 1903).

Case of symmetrical gangrene present at birth in a girl with a congenital valvular defect. Barnwater (Wiener klin. Woch., Feb. 19, 1925).

**CARBOLIC ACID GANGRENE.**—Carbolic acid has caused gangrene in so many cases that it seems to merit a special place among chemical agents capable of inducing this condition. Even in 2 per cent. solution, this agent is capable of destroying the life of tissues. The majority of cases reported in which gangrene occurs were felons or slight disorders of the finger-tips or toes. According to Czerny the duration of the application is more important than the strength of the solution, the anesthetic action of the drug causing it to be left *in situ* prolonged periods at a time. The parts first become grayish white and eventually black. There is no pain, and the gangrene is only revealed by the appearance and the stiffness of the finger or toe affected.

Eighteen cases of gangrene of the fingers, the result of weak carbolic acid dressings. This makes a total of 132 cases reported. Carbolic acid in any strength as a moist dressing is dangerous, and should never be used. F. B. Harrington (Amer. Jour. Med. Sci., July, 1900).

Nine cases of gangrene of the finger or fingers, due to the application of carbolic acid dressings. In 7 out of the 9 cases, amputation was required. In 4 of the cases the strength of the solution used was not over 5 per cent. In none was a waterproof covering used, nor had there been any constriction by a bandage. The appearance of the gangrenous part is characteristic. The skin is at first dry, wrinkled, and grayish white in color; later it becomes darker and more shrivelled. At the junction of the living and dead tissue there is some hyperemia, and eventually a line of demarcation forms. This should always be waited for before amputation is performed. Wallace (Brit. Med. Jour., May 11, 1907).



Carbolic Acid Gangrene of Finger     *Chas. A. Kelly.*  
Annals of Surgery



The writer condemns the sale of carbolic acid to the public, warns the physicians who use carbolic acid in the form of moist compresses that unpleasant results not infrequently follow its use, and suggests a new factor, possibly two, in the production of carbolic acid gangrene of the fingers and toes: 1. The mechanical constriction to the circulation, due to the contracted and hardened skin, which acts like a tight bandage applied to the part. 2. The possibility of a sclerotic artery, which is not uncommon in the young, playing a part in some of these cases, as it undoubtedly did in the case which he describes. Leighton (*St. Louis Med. Rev.*, Feb., 1909).

In cases of phenol gangrene of the fingers, **amputation** is formally called for, as otherwise serious septicemia is liable to be entailed. In a case the writer describes, the woman of 50 had applied a 5 per cent. solution of phenol to her finger, keeping it constantly moist for 24 hours. Besides the gangrene, there were hallucinations, excitement and delirium as with high fever, but there was no fever and the pulse was regular and strong when he saw the woman the twentieth day. She died in collapse the twenty-second day. R. Le Clerc (*Bull. de l'Acad. de Méd.*, Paris, Feb. 25, 1919).

#### ETIOLOGY AND PATHOLOGY.—

The causes of tissue-death are divided by Tillmann ("Surgical Pathology," Rogers's transl.) into four general classes: 1. Interruption of the efferent flow of arterial blood without the development of a collateral circulation, such as may occur in the cases of thrombosis and embolism, or after ligation, or in consequence of the pressure of a tumor or inflammatory exudate. 2. Interruption of the afferent flow of venous blood. 3. Interruption or stasis of the circulation in the capillary walls. 4. Death of the tissue-cells without any disturbance of circulation, due to poison, such as snake-bites, or to micro-organisms or the products of their metabolism, such as are found in infectious-complications of wounds, *e.g.*, erysipelas, cellulitis, and septicemia, or, finally, to local anesthesia.

The writer observed 2 cases of gangrene after local anesthesia; in 1 the great toe became gangrenous four days after an operation under local anesthesia for an ingrowing nail. In the other case a hydrocele was operated on under novocaine-adrenalin and gangrene of the scrotum developed. Strohe (*Deut. Zeit. für Chir.*, July, 1909).

Gangrene of the uterus following criminal abortion is emphasized by the writer. Serious trouble may follow the introduction of irritating solutions or unclean instruments, owing to gangrene of the wall of the fundus, a small perforation, etc. He cites 4 such cases. Mauclair (*Ann. de gynéc. et d'obstét.*, xlii, 193, 1916).

Case of gangrene of the entire back of the head in a woman of 26 who had had her red hair bleached 10 days before. The label on the bottle specified 30 per cent. hydrogen dioxide. The woman, subject to eczema, wore a felt hat home, thus steaming the region further with the fumes of the chemical while the braids of hair were pressed by the hat on the irritated scalp. The pain was so severe as the woman walked home that she fainted. The region healed over in the course of 3 months, leaving a cicatricial bald area, 9 by 10 cm. in size. Von Berde (*Dermat. Woch.*, Feb. 20, 1926).

Local and general anemia, venous stasis, disturbances of circulation from diseases of the vessels, heart or lungs, or disturbances of circulation due to inflammation—in short, faulty circulation from any cause—increase the disposition to gangrene from the effects of chemical or thermal influences.

The special etiological factors have been already alluded to, while gangrene as a complication of various infectious diseases has been reviewed in the respective articles upon the latter.

Study of 15 specimens of gangrene. In cases due to arterial sclerosis a high grade sclerotic proliferation of the intima is found, causing stenosis of the lumen of one or more of the main vessels. It threatens the life of the

extremity by closing the exit of the branches from the vessel involved, preventing the formation of collateral circulation. A secondary progressive thrombosis is also apt to develop on the changed arterial wall. Senile or diabetic gangrene, a localized petrification of the arteries, sometimes forms. Bunge (Archiv f. klin. Chir., Bd. lxii, H. 1, 1901).

Analysis of personal cases and of all the cases of gangrene following infectious disease found in literature: 166 in all. The most frequent causes were typhoid and typhus fever, and after these influenza, puerperium, and pneumonia, in the order named. Scarlet fever was the cause in only 3 cases, and diphtheria in only 1. The commonest seat is in the legs, 122 cases having gangrene in this situation. There appears to be no difference between the right and left legs, and gangrene of both legs is less common than of either separately. In 128 cases of which the result is known, 42 patients died. The percentage is much higher among women than among men. In 65 cases autopsy showed thrombosis in the main artery of the limb. In many of the others investigation was not made. Eichhorst (Deutsches Archiv f. klin. Med., vol. lxx, H. 5-6, 1901).

Rapidly spreading gangrene, the *gangrène foudroyante* of French surgeons, is developed when to a necrotic process in the economy there is added a rapidly spreading emphysematous condition of the surrounding parts, with increased tension, crepitation, the formation of gaseous bullæ, and a bronzed and streaky discoloration of the skin. The disease, once established, tends to spread rapidly to other parts of the body, and constitutes the most fatal form of gangrene.

Gaseous gangrene may be produced by various micro-organisms, particularly, however, by the *Bacillus aerogenes capsulatus*, which, without having a specific action, behaves in man as a toxin saprophyte upon tissues already seriously damaged. The *Bacillus coli communis*, with other germs, may also cause gaseous gangrene. Muscatello (Rif. Medica, May 21, 22, 23, 1900).

Case of gaseous gangrene in a non-diabetic person, in which the bacterium coli was the sole agent isolated. This germ cannot, however, produce gaseous gangrene alone; its action is then entirely saprophytic and is dependent upon other pathogenic organisms, or upon local or general nutritional disturbances, such as trauma and metabolic diseases. Dansauer (Münch. med. Woch., Sept. 8, 1903).

*Infectious gangrene* of the skin is occasionally observed. According to Caillaud this appears under two conditions: There may be a previous ulcerative skin-lesion, from and upon which the gangrene starts, or the gangrene may appear immediately after a non-ulcerative manifestation of the skin; it is not an occasional accident, but constitutes an essential element of the disease. Any cause which impairs general health predisposes to that contagious affection, and existing ulcerations and erosions serve as a door of entrance for the contagion.

Case of a little girl, aged 19 months, who was suddenly taken ill with vomiting, diarrhea, tenesmus, fever, and convulsions. On the following day a small blister was found on the right nate. Others appeared elsewhere, increased in size, and turned dark red. Death followed. Smith (Jour. Kans. Med. Soc., Feb., 1907).

The writer observed in Odessa an epidemic of acute gangrene of the external sex organs in little girls. Various infectious diseases had preceded the gangrene. Stephany (Deut. Med. Woch., Mar. 7, 1924).

Spreading traumatic gangrene, though usually developed in subjects suffering from general depraved health, occasionally occurs in healthy subjects through infection of the wound by the anaërobic bacillus of malignant edema of animals, and to which fowls are particularly susceptible. Through the experimental observations of Chauveau and Arloing, Brieger, Ehrlich, and others, the fact has been practically established that the same germ, which, on the one hand, may give rise in animals to malignant edema, may, on the other, when grafted in man on tissue the seat of a moist gangrene, produce the emphysematous condition.



In the field-mouse, an animal immune to the bacillus of septicemia, Koch produced, experimentally, a progressive gangrene from inoculations with chain micrococci not to be distinguished from the *Streptococcus pyogenes*. He also pointed out that the ptomainic products of bacterial activity may themselves cause the destruction of tissue, since, in the examination of specimens from the inoculated animals, the progressive necrosis was observed markedly in advance of the bacterial invasion.

Case of gaseous gangrene complicating a compound fracture of the right forearm in a boy of 10 years, the bones coming in contact with mud. For the first two days the patient did well, then the arm began to swell and became rapidly emphysematous and gangrenous, with a line of demarcation an inch above the elbow; the swelling was dusky in color and there was crepitation extending over the scapula and below the clavicle. Several long incisions were made along the forearm and gas escaped with great force. Antiseptic measures were carried out and the condition of the arm rapidly improved, probably because of the relief from pressure on the blood-vessels by the gas. Amputation at the junction of the upper and middle third of the arm was necessary, however. The condition is believed to have resulted from infection with the *Bacillus aerogenes capsulatus*, but no bacteriologic examination is reported. Reports of 16 cases of infection by this micro-organism in literature, with 12 deaths and 4 recoveries, found. C. P. Gildersleeve (Med. Record, March 4, 1899).

The writer observed a case of gangrene of the right foot and leg following septic abortion due to a mixed infection of *B. aerogenes capsulatus*, streptococcus and a diplococcus, starting as a thrombophlebitis of the right broad ligament, and involving the inferior vena cava. Knipe (American Journal of Obstetrics, June, 1917).

**TREATMENT.**—Removal of the causative factors and especially those interfering with free circulation is the first indication.

In strangulated hernia, section of the constricting ring brings about this result; in paraphimosis, pressure from superficial tumors, bed-sores, tight bandages, etc., relief can be afforded also by overcoming the constriction. In many cases, however, this is not possible. In obstruction due to thrombosis and arteriosclerosis, for example, everything should be done to facilitate the return of the blood by judicious procedures. In purely thrombotic cases, **hypodermoclysis** or intravenous infusion of **saline solution** to increase the fluidity of the blood may prove useful. **Elevation** of the part, with **slight flexion** of the **extremity affected**, gentle **massage** toward the heart, **warmth**, taking care to avoid "hot-bottle burns," which under such circumstances are easily inflicted, represent the minor indications.

The writers obtained good results with small doses of **pilocarpine** and **insulin** in the treatment of spontaneous gangrene. Stuhlern, Agulowa and Babbkova (Med. Klinik, Nov. 20, 1925).

**Amputation**, the sole effective measure hitherto available in dealing with cases of diabetic gangrene due to obliteration of the arterial supply, is itself attended with danger, the organism already being placed in jeopardy because of the absorption of toxins. Dieulafoy found that by the employment of currents of **air heated** to 150°, 300°, 500° C. or even higher, extension of the gangrene and toxic absorption could both be arrested. On repeated use, such currents produce carbonization of the part and limit the gangrenous process by keeping the tissues dry. Extension of the process and infection having been checked, **amputation** can with safety be performed and the patient rid of the necrosed segment of limb. Marked success was obtained in the cases thus treated.

Case of a man 64 years old, whose urine showed 82 Gm. of sugar in the twenty-four hours, with albumin and acetone. **Hot air** treatment was begun at once and continued twice a day half an hour at a time—air at 300° C. on the portion below the line of demarcation, at 80° to 100° on the living tissues above it. The patient began to improve at once.

The sugar decreased steadily, the acetone also; the temperature of the air-douche was raised to 400°. The leg mummified. Gradually a deep line of separation formed at the garter, which was followed up closely by the **hot-air douche**, and finally all the posterior tissues separated spontaneously, leaving the bones bare. Dicalafey (Bull. méd., Feb. 16, 1910).

In the obstetrical tears which suppurate and show tendency to gangrene, the writer has obtained excellent results by application of **super-heated air**; it penetrates into all the infected crevices and destroys the putrefying tissues. Dupont (Annales de gynéc. et d'obstét., July, 1910).

In inoperable peripheral gangrene, the writer strongly recommends **dry hot air** to relieve pain and stench and mummify the tissues. Air heated to about 150° F. may be directed through a small stove pipe from a Bunsen burner to the part. W. G. Thompson (Med. Rec., Dec. 23, 1916).

When, notwithstanding prophylactic measures, the gangrenous process develops, disinfection of the area should at once begin. **Iodoform, orthoform, aristol, and resorcin** are valuable in this connection.

Remarkable results obtained in a diabetic who had had gangrene in one leg which necessitated amputation. The other leg became involved, and a succession of scabs formed on the foot. No pulse could be felt in the dorsal artery of the latter or in the posterior tibial. After a half-hour's **massage** the whole foot and leg were warmer, the tissues softer, and the tension less, and the dorsal artery could be felt so that the pulse could be counted. The method of work was principally by deep manipulation in a downward direction to aid the arterial current, followed by upward friction, or effleurage, to aid the venous and lymphatic flow. Douglas Graham (Inter. Clinics, vol. iv, series 10, 1901).

The next object is to prevent infection of the healthy tissues beyond by products of decomposition. Any accumulation of offensive fluid or gas should be prevented by

evacuating foci and treating the part with antiseptic lotions. An excellent agent in this connection is **permanganate of potassium** in 1-grain-to-the-ounce solution. Infiltration abscesses should be followed up to the living tissues above, if needed, to thoroughly clear them of the infecting elements. Carbolic acid should not be used as a disinfectant, since it tends to lower the vital resistance of the tissues and to promote gangrene.

In severe wounds of the extremities in which gangrene is threatened, as evidenced by cyanosis and coldness of the distal part, the author believes that the gangrene results from stasis of the blood. In order to promote the circulation, he recommends one or more small **incisions** in the **cyanosed area**, application of a **camphor-oil dressing** (to prevent drying), and placing the extremity in a **suction apparatus** at a negative pressure of between 12 to 15 cm. for eight to ten minutes. This is done two or three times a day for a week. It will be noticed that arterial blood exudes which increases in quantity day by day. The color slowly improves, the sensibility of the part returns, and the wound heals nicely. In a number of cases the writer believes that he has saved portions of an extremity which would otherwise have been lost. H. Noesske (Centralbl. f. Chir., Oct. 2, 1909).

Case which confirms anew the great value of stimulating the capillary circulation by **Noesske's method** of cutting down to the bone at the tip of the finger parallel with the nail. Fehsenfeld (Munch. med. Woch., Oct. 29, 1912).

The adoption of radical measures must be regulated by the progress of the case and the nature of the primary disorder present.

In a case of diffuse phlegmon of the leg with gangrene the writer used successfully: 1. Linear applications of **thermocautery**. 2. Subcutaneous injections of **hydrogen peroxide** 1 to 2 centimeters above infected area. 3. **Passive hyperemia** induced thrice daily by rubber bandage above knee. 4. Daily bathing of part in warm

**permanganate** solution. 5. Wet dressing of hydrogen peroxide. H. Petit (Arch. de méd. militaire, No. 12, 1909).

Extensive and deep shell wounds of the forearm were found to contain gangrenous, both aerobic and anaerobic, germs. Under continuous moistening with Dakin's fluid the dead tissues melted off, no slough forming. The main property of the **Dakin fluid** is this chemical detergent action. A 5 per cent. solution of sodium chloride checks the dissolving action of hypochlorites. Applied around the wound it prevents caustic action. Fliessinger and Moiroud (Paris méd., Sept. 16, 1916).

**Arteriovenous anastomosis** has been tried by Hubbard with improvement as result. The foot, originally purple, appeared almost normal, with the exception of the toes. The measure has not been applied with sufficient frequency to render a verdict as to its value possible.

Series of 4 cases of senile gangrene in which the writer tried **anastomosis between the femoral artery and vein**. No benefit was observed, the lesions being too far advanced. Maucclair (Arch. gén. de chir., Aug. 25, 1913).

Report of 2 cases, with 1 recovery, of **removal of emboli** from the brachial artery. In the first case the operation was done over 6 hours and in the second  $3\frac{1}{2}$  hours after the evidences of arrested circulation in the limb were first noticed. Local anesthesia was used in both instances, and the arteriotomy incisions closed by the Carrel technic. Buerger (Surg., Gynec. and Obstet., Apr., 1923).

It is generally thought advisable not to interfere with the reparative efforts of nature when the line of demarcation is clearly established. When, however, in the case of an extremity, there is no line and the morbid process ascends here and there or evenly and the patient shows evidences of impending constitutional disturbances, the question of **amputation** is in order. In arriving at a decision in this connection the various reasons for an amputation should be carefully computed, namely: The nature of

the causative disorder; the probabilities as to spontaneous resolution; the subsequent deformity involved, both without and with amputation based upon the parts (muscles, nerves, vessels) already destroyed; and last, but not least, the general health of the patient. These may all prove useful in case of subsequent controversy. Severe injuries followed by gangrene warrant amputation if the tendency to spread is evident. When a putrescent mass, however, though the line of demarcation be present, exposes the patient to general toxemia, amputation is also warranted as soon as the signs of septicemia appear. Especially is this true in "traumatic gangrene."

All surgeons agree that a high amputation is to be preferred, and the knee or thigh is usually selected because the profunda femoris is rarely obstructed by thrombi.

When **amputation** is determined upon, the anatomical distribution of the vascular supply of the part must clearly be borne in mind and an effort made to leave in the flaps, not only unobstructed vessels, if arteriosclerosis or thrombosis be present, but also a sufficient supply to insure proper nutrition.

We possess no means of establishing at what level the vessels of the leg are in a healthy state, i.e., where to amputate. In order to determine the state of the vessels, the writer recommends that the affected leg be rendered bloodless by means of an Esmarch bandage, and that the bandage then be suddenly removed. In a healthy leg sudden removal of this sort is followed by an active red hyperemia extending to the tip of the toes, whereas, if the vessels are diseased, the hyperemia occurs more slowly and usually extends only as far as that point where the vessels are in good condition. The writer quotes 3 cases in which amputated legs were studied with the result that the preoperative diagnosis was absolutely confirmed. A. Moszkowicz (Mitt. a. d. Grenz. d. Med. u. Chir., Bd. xvii, H. 1 u. 2, 1908).

Smith recommends the following amputation when gangrene of the foot is present, and when it is decided to amputate at the knee or through the thigh. There being

eight arterial branches in this region, if the incisions and flaps are suitably planned this arterial supply need not be seriously interfered with. His method of amputation is as follows: A straight incision is made from two inches above the upper border of the patella downward over the center of that bone to the tuberosity of the tibia. From the lower extremity of this perpendicular incision two curved incisions are made, having their convexity downward, and extending, respectively, in the direction of the external and internal borders of the limb. These two incisions having been united posteriorly by a straight incision across the upper border of the calf, the flaps are dissected up from the tibia and fibula, the patella is removed, and the knee-joint is disarticulated.

In *senile gangrene* a conservative line of treatment is indicated, since meddling surgery here is liable to be followed by extension of the morbid process. Attention to the healthy tissues of the entire surface is necessary, since a minute abrasion, a slight blow, may become a gangrenous area. As taught by Jones, when the gangrene affects one or two toes and the patient's condition is satisfactory, the surgeon should be content with the expectant plan of treatment, taking precautions to lessen or prevent the effects of local septic infection. When, however, the gangrene has reached the metatarsus, he should be prepared to perform the high operation, *i.e.*, amputation above the knee.

The local treatment in limited forms of gangrene should consist in thorough cleansing of the foot and leg, free dusting of the immediate vicinity of the dead part with **iodoform**, and the application over this powder of **sublimate** or **salicylic wool**. The use of artificial heat in the form of poultices and fomentations is positively mischievous. Pain may be relieved by the internal administration of **opium** and the local application of a powder composed of **boric acid**, **bismuth subnitrate**, and **morphine hydrochloride**.

The writer observed 20 cases of *senile gangrene* all subjected to operation. In 19 cases an amputation was done above the knee on the affected side; in 1 case an amputation was done below the knee. The oldest patient operated on was 83 years of age; the

youngest, 56. Eighteen patients were men and 2 were women. Eighteen patients recovered; 2 died. Of 11 patients with capillary thrombosis, 10 recovered; of 4 patients with primary obstruction of a large artery, 3 recovered; of 3 with diabetes complicated by gangrene, 3 recovered; of 2 with gangrene associated with inflammatory and toxic conditions, 2 recovered. Noon (*Pract.*, Dec., 1925).

In the treatment of *diabetic gangrene* no special features are indicated. Heidenhain, who has given the subject special attention, states that, as in *senile gangrene*, as long as the gangrene is confined to one or two toes the line of demarcation should be awaited and the dead tissues allowed to separate of themselves. Removal of the gangrenous portion with forceps and scissors may lead to gangrene of the parts above, although the line of demarcation has been fully established. As soon, however, as the gangrene attacks the sole or the dorsum of the foot, an **amputation** of the thigh should be made as close above the condyles as possible. Amputation below the knee is nearly always followed by gangrene of the flaps.

In 11 cases of *diabetic gangrene* 6 were saved by thigh amputation; 2 of the 3 fatal cases had large quantities of sugar in the urine (8 per cent. and 5 per cent.), while the remaining 2 showed much albumin in addition to sugar. Such cases should avoid even insignificant injuries, which in them may assume serious proportions—precisely as in *senile gangrene*.

*Symmetrical gangrene* rarely calls for surgical interference. The treatment of the neurosis and constitutional measures are generally sufficient.

#### CONSTITUTIONAL MEASURES.—

These should not be neglected. Nutrition should receive especial care, and the patient should be supplied with nourishing food. The low diet which older ideas seemed to warrant belongs to the past. **Alcoholic stimulants** should be given, but in small quantities at a time—just enough to sustain normal cardiac action. **Strychnine** is a valuable adjuvant, by stimulating vasomotor action. Promiscuous drugging should be avoided. **Hypodermoclysis**, or, better, **saline solution** intravenously, arc, however;

rational measures, their purpose being to increase the fluidity of the blood.

**GANGRENE DUE TO SYPHILITIC ENDARTERITIS.**—Lesions in the blood-vessels in the secondary period of syphilis are, according to Ravogli, the result of a hyperplastic inflammatory process, and in the tertiary period represent a true gummatous infiltration. It has been shown that the spirochetes circulating free in the blood attack the epithelial lining of the vessels, causing alterations in them. Several observers have found spirochetes in large colonies in the vascular tunics. The organisms have also been detected in the superficial network of inflamed capillaries. In the arteries the adventitia is scarcely distinguishable from the other tunics, the media appears smaller and compressed, while the intima is thickened and interwoven with hyperplastic young cellular elements concentrically disposed. The lumen of the artery is diminished and altered in shape; often it is occluded by a thrombus. According to the vessels involved three forms of gangrene may be produced: 1. *En masse*, when the principal artery of a limb is occluded, oftenest due to endarteritis in the late stage of syphilis. 2. Superficial, the result of an acute endo-angeitis in the small arteries supplying an area of skin. 3. In the center of deep syphilitic lesions, due to pressure of the infiltrating elements on the blood-vessels and tissues.

Three cases of syphilitic gangrene. In the first, gangrene began in the toes and spread upward to the whole foot, malleoli, and knee. On amputating at the thigh, the femoral artery was found rigid and occluded by a thrombus. The gangrene continued and death occurred from sepsis. The second case presented a superficial gangrenous condition of the external region of the whole left thigh, extending to the upper third of the leg. Sloughing took place after a few days of local treatment (continuous baths of 1:10,000 bichloride of mercury), and the area gradually healed. In the third case, a gumma of the lower lip developed into an extensive gangrenous mass, further progress of which was arrested by deep injec-

tions of 1 per cent. bichloride of mercury solution, large doses of potassium iodide, and locally a moist dressing of 1:5000 bichloride. The surface healed, leaving a bad scar, which was corrected by a plastic operation. Heroic antisiphilitic treatment is necessary in these cases, the gangrenous process having been checked thereby in several instances. Especially when the syphilitic process has acted on the small vessels can limitation of the gangrene be obtained. In all the cases tonic treatment, particularly quinine in large doses, was found of great value in subduing septic conditions. A. Ravogli (Lancet-Clinic, Feb. 12, 1910).

The writer gave neoarsphenamin intravenously in 12 cases of genital gangrene. The effect on the temperature and the course of the process was so prompt and so constant that this treatment should be given at once in every case, regardless of the temperature or general symptoms. Jersild (Ugeskrift f. Læger, Oct. 8, 1925).

**GAS GANGRENE.**—This form of gangrene was exceedingly prevalent during the war. The symptoms, according to Fauntleroy (Annals of Surg., Jan., 1916), are as follows: After 2 to 5 days there is swelling, with gas in the tissues and induration of the skin; a brownish discoloration is noted, and a fetid odor is characteristic of the serosanguinous discharge from the wound. More or less suddenly, vesicles appear, varying in size from a pea to several inches. The pulse distal to the wound becomes weaker and in the last stage is absent. The fluid in the vesicles rarely contains the organism. Injuries predisposing to gas infection are usually associated with shock and sapremia, and in 10 to 30 hours the specific invasion causes a rise of temperature of 1 or 2°, rise in pulse-rate, headache, malaise, anorexia, and thirst. The second stage is marked by progressive gas formation, circulatory disturbances, and increased virulence. The pulse-rate increases out of proportion to the temperature, which may reach 104° or 105° F. (40° or 40.6° C.). The discharge increases, the part swells,

crackling is marked, there is mottling of the skin, and the patient passes into a fitful coma heralding the final stage, septicemia. There is then a falling temperature curve and rising pulse-rate.

As to the incidence of this wound complication, G. Gross (Bull. de l'Acad. de méd., Paris, lxxvi, 586, 1916) stated that out of the 2796 severely wounded men received in his ambulance during the battle of Verdun, there were 101 cases of diffuse, massive, gas gangrene, 92 due to shell wounds. Leg injuries were those oftenest complicated by gangrenous septicemia. Vascular lesions play an important rôle. The results were 44 recoveries and 57 deaths, after either amputation, disarticulation, or a wide opening up, with ether treatment. Among those operated within 12 hours the mortality was only 4.8 per cent.; in those after 36 hours, 26.88 per cent.

**Diagnosis.**—Gas infections of war injuries were divided by Lapeyre (Presse méd., p. 431, 1916) into (1) Gaseous septicemia, appearing very early, with local and general disturbances, and a rapidly fatal course. There is no true clinical gangrene, and death usually occurs in 30 to 50 hours. (2) Gaseous gangrene, less grave, yields to surgical treatment. It seldom appears before the third day. The signs are edema, fetid gas, and sphacelated areas about the wound or in the whole limb segment. This form may be gaseous, edematous, or gangrenous according to the predominating symptom.

Crepitations can be detected by auscultation with a stethoscope of the portion of the limb infected with gaseous cellulitis. While this sign is present in a well-established case with "dummy muscles," its importance lies in the fact that it is present in a number of cases before the muscle becomes resonant to percussion. The sign is produced by placing the stethoscope on the swollen part and then alternately increasing and decreasing the amount of pressure applied to the chest-piece; this produces the necessary movement of the underlying muscle. B. C. Maybury (Jour. Royal Army Med. Corps, Jan., 1918).

H. Black (Brit. Med. Jour., Jan. 6, 1917) found the X-rays of diagnostic advantage in the less malignant forms of gas infection. The gas shows as areas of lessened density varying in size from 1.5 to 3 cm. H. M. Berry (Proc. Roy. Soc. Med., x, Sect. Electro-Therap., 17, 1916) noted that in all cases of diffuse gas infiltration shown by the X-rays crepitation of the tissues could be felt. Where only a few discrete gas bubbles were shown, nothing abnormal was palpable.

**Etiology.**—In 460 cases of gas infection studied by M. H. F. Ivens (Med. Press and Cir., Jan. 13, 1917), of which 107 were clinically gas gangrene, the leading etiological factors were as follows: Proximity to contaminated soil; wounds of the lower limb showed a mortality 3 times as great as those of the upper, though the latter were more frequent; shell wounds were 6 times as frequent in gas gangrene as in ordinary infected wounds; the presence of an infected fragment of great-coat kept up the infection. Early wound treatment is most important in the prophylaxis. Sixty per cent. of gas infected cases had fractures, and 71 per cent. of gas gangrene cases. Deep wounds of the calf, trunk, or hip-joint were especially dangerous. Tissue injury had an important influence, and intramuscular tension from within or without was a potent aid to the production of gangrene. The flora of gas gangrene was found usually multiple in 464 cases. *B. perfringens* was present in nearly every case; *B. sporogenes* in 41; vibriion septicus in 6 (several fatal); *B. histolyticus*, *B. Hibler IX*, and *B. edematiens* were all reported, less frequently. Streptococci of a virulent type were present in 59 cases, and added to the gravity of the infection. Tetanus occurred in 15 cases. Of the 464 cases 42 were fatal, 25 dying from gas gangrene, 4 from tetanus. M. Weinberg (Glasgow Med. Jour., Apr., 1916) pointed out that most of the organisms related to gas gangrene belong to the intestinal flora.

The writer observed gas gangrene after injections of caffeine and digitoxin in an athletic man with purulent peritonitis. Gas bacilli were found in the solutions. It is remarkable that 6 other patients who had been given in-

jections of the same fluid, but were in a better general condition, remained healthy. Heuss (Med. Klinik, Mar. 27, 1925).

According to W. d'Este Emery (Lancet, May 6, 1916), *B. perfringens* is a frequent contaminating organism in wounds, but in most cases it fails to produce gas gangrene, and seems non-pathogenic, probably because it is readily destroyed by normal blood, and is strongly chemotactic toward leucocytes, which promptly destroy it. The special conditions leading to its rapid development are those resulting in tissue destruction and interference with local circulation. J. P. Simonds (Jour. Exper. Med., June, 1917) found spores of the *B. welchii* group of bacteria in all uniforms of Belgian soldiers and in all samples of new cloth from which the uniforms were made; also in 15 out of 20 fresh war wounds. But 3 of the wounded developed gas gangrene. Deep lying lacerated muscle tissue seemed the most frequent seat of gas gangrene.

The writer isolated the *Bacillus multifermentans tenalbus* from a case of gas gangrene of the arm and subjected it to careful bacteriological investigation. The various cultural characteristics of the organism are given in detail and it is pointed out that in some respects it resembles the *Bacillus vibron septique*, from which it is, however, distinguished by definite differences in the characters of its colonies, and in its morphology, serology and pathogenicity. It has been named with reference to its main features—the multiplicity of its fermentation reactions and the tenacious, white colonies it produces. It does not appear to be pathogenic when inoculated alone into animals, but when combined with the *Bacillus sporogenes*, both it and the latter organism become pathogenic. In the human case from which it was originally isolated it was found in combination with the *Bacillus sporogenes*. Excision of the gangrenous muscle was followed by prompt recovery of this patient. J. L. Stoddard (Lancet, Jan. 4, 1919).

**Pathology.**—From a clinical and histological study of 11 cases C. Wallace (Brit. Med. Jour., Sept. 16, 1916) stated that the lesion in its early stages is a longitudinal one, running up and down the injured muscles. Direct extension to an intact muscle is rare, except when pressure becomes sufficient to interfere with its blood-supply. Muscles in rigid compartments are especially prone to die, if wounded. The muscles become resonant from gas long before they become crepitant to the finger. Yet crepitation may be perceptible early with the stethoscope.

A chemical study of the blood and urine in gas gangrene with a view to ascertaining which factors counteract or favor toxemia of anaerobic origin, showed that in heavily infected gangrene cases a marked hypoalkalinity of the blood was always found. The hypoalkalinity was proportionate to the intensity of the infection; the lower the alkalinity the more unfavorable the prognosis. Oliguria was regularly noted, and in certain cases terminating fatally, anuria. The urine showed slight hyperacidity. Marquis, Clogne and Didier (Presse méd., Dec. 5, 1918).

**Treatment.**—Fraser and Bates (Brit. Med. Jour., Aug. 5, 1916) treated 7 cases of gas gangrene by intravenous injections of **hypochlorous acid**. Four recovered. Of the remaining 3 but 1 could be regarded as an inexplicable failure. The solution employed was **lusol**, containing 0.5 per cent. of hypochlorous acid, to which was added 8.5 grains (0.55 Gm.) of sodium chloride to the liter (quart). The injection is made with a syringe, to the amount of 40 to 70 c.c. (1½ to 2¼ ounces).

The hope of benefit from oxygen has had to be abandoned, according to Tansini (Policlinico, May 6, 1917), but good results have been obtained in many gas cases by **prompt excision** into sound and bleeding tissue. One should refrain from severing an entire muscle or group of muscles, but they can be slit over long distances with little harm. According to C. Wallace (Brit. Med. Jour., Sept. 16, 1916), the circulation should be preserved when possible, and helped in every way. Ten-

sion from effusion or gas should be relieved by **free incision**. **Incision**, or **ablation**, of the **wounded muscle** is often sufficient to arrest the disease. G. Campora (Gaz. degli osped. e delle clin., May 28, 1916) advised **destruction** of the primary **focus**, **free incision**, **disinfection with hydrogen peroxide**, **potassium permanganate** or **iodoform** and **ether**, followed by pursuit of the infection along its paths of diffusion, and **free incisions**, combined with **irrigations of peroxide**, and **drainage** with gauze moistened with it.

In 100 severely infected cases of gas gangrene which had been treated with Dakin's solution for 10 days or longer without any appreciable signs of improvement, the writer used **quinine sulphate**, 1 Gm. (15 grains); **hydrochloric acid**, 0.5 c.c. (8 minims); **glacial acetic acid** (99 per cent.), 5 c.c. (80 minims); **sodium chloride**, 17.5 Gm. (4½ drams); solution of **formaldehyde**, 1 c.c. (16 minims); **thymol**, 0.25 Gm. (4 grains); **alcohol** (90 per cent.), 15 c.c. (½ ounce), and water, to make 1 liter (quart). The preparation was compounded as follows: (1) Dissolving the quinine in the hydrochloric and acetic acids; (2) dissolving the sodium chloride in the water, and (3) dissolving the thymol in the alcohol. No. 1 was added to No. 2, then the formaldehyde, and finally the thymol solution. Pilcher (Ann. of Surg., Jan., 1925).

Weinberg and Seguin (Presse méd., Feb. 22, 1917), who discovered the *Bacillus edematiens* in 1915 in certain toxic forms of gas gangrene and in one-third of the cases of gas gangrene terminating fatally, found it in wounded subjects from all points on the military front. Next to the tetanus bacillus, it is the most violently toxic organism in wounds. They have prepared an **anti-edematiens horse serum** with antitoxic and prophylactic properties approaching those of diphtheria antitoxin. While its prophylactic is much more pronounced than its curative power, it was used with success among wounded men in a few cases.

Having observed the curative value of the **antiperfringens serum** prepared

by Weinberg and Seguin at the Pasteur Institute, the writer tested its preventive use. From March 21 to September 6, 1918, 3660 recently wounded received their first operative treatment in the hospitals under the writer's care. He employed in 3 series of cases: (a) the **mixed serums** antiperfringens, antivibrio septique, anti-edematiens, prepared by Weinberg and Seguin; (b) the polyvalent serum of Leclainche and Vallée; (c) a combination of the two.

Antigangrenous serums were given preventively in 433 cases, all of a severe type, including nearly 300 fractures, many cases already presenting one or other of the clinical signs of gas gangrene, such as crepitation, discoloration of muscle, bronzing of skin, edema, and bad odor. A large number were cases of wounds of the lower limbs. Nearly all patients were received within the first 24 hours after being wounded. By giving serum subcutaneously in dilution the writer believes he averted the anaphylactic phenomena which have been observed in cases in which this method of procedure has not been followed. When the mixed serum was given at or before the first operation (222 cases), no patient died from gas gangrene, although there were 19 deaths out of the number from the effects of shock, from multiple fractures, hemorrhage, meningitis, or streptococcal septicemia. In 14 of these cases the serum was administered at the same time that amputation was performed for massive gas gangrene. Of these 14 patients, 12 recovered. The 2 fatalities occurred at the end of a fortnight from streptococcal septicemia, all signs of gas gangrene having disappeared for more than a week. In a very large number of cases the administration of mixed serums permitted conservative treatment to be adopted instead of the amputation which would otherwise have been inevitable. F. Ivens (Brit. Med. Jour., Oct. 19, 1918).

The improved methods of rapid evacuation of the wounded and early



surgical intervention have brought the cases of gas gangrene down to 0.29 per cent. of the wounded at the advanced posts; 0.19 per cent. in the intermediate zone, and 0.30 per cent. in the interior. Gas gangrene developed in the hospitals of the interior only in 0.068 per cent. of the men who had been operated on before. Aside from the wounded lying too long on the field untended and those with shock too severe to permit operation, it seems that gas gangrene can be avoided, even without specific **serotherapy**. Among the improvements realized is the recognition that crushing of muscle tissues invites gas gangrene, as also ligation of too many arteries. Surgeons now do not shrink from long incisions and extensive resection of lacerated tissues in such cases. Antigangrene serotherapy has given encouraging results. Sieur and Mercier (Bull. de l'Acad. de méd., Oct. 29, 1918).

The writer used a serum against the perfringens and edematiens organisms and the septic vibrio. The **mixed serum** was found to be well borne. Prophylactic administration of the mixed serum is advised in all severe wounds of the extremities, with or without fracture, especially in the presence of injuries to large vessels. The mixed serums being well tolerated, it might even prove advisable to administer 20-c.c. (5-dram) doses of each of the serums separately. Where a rapid influx of wounded or the poor general condition of the individual himself prevents prompt surgical treatment, the prophylactic serum injections should be repeated for several days. E. Vaucher (Presse méd., Jan. 3, 1918).

The use of **serotherapy** in 191 cases of gas gangrene gave recovery in 86.91 per cent. In 113 instances the gas gangrene was well under way when serotherapy was begun, but 83.08 per cent. recovered under it. Serotherapy thus has proved useful in both prophylaxis and treatment. Sacquépée and De Lavergne (Presse méd., Feb. 20, 1919).

Out of 191 cases of gas gangrene treated with **serum** against the *B. bellonensis*, *B. perfringens*, and *vibrio septicus*, the writer obtained 166 recoveries, the mortality being thus 13 per cent. as compared with 75 per cent. in untreated cases. Prophylactic serum treatment in cases in which the disease is apt to develop is also of great value, but 1 per cent. of those treated developing the disease, as against 7 per cent. among the unprotected. Sacquépée (Lancet, excix, 605, 1920).

The writer treated successfully a case of gas gangrene of the thigh following an accident by the injection of three large doses, 100 c.c., on consecutive days, of a **serum** representing a **mixture of Welch's perfringens form of the gas bacillus with tetanus**. C. Goodman (Ann. of Surg., June, 1924).

Albrecht (Berl. klin. Woch., July 27, 1916) stated that some cases resist even the most radical treatment, showing yellow pallid tint, anguished facies, pale cyanosis of the lips, profound agitation, and terrible pain, death following rapidly, due to direct action of the toxin on the heart. He examined the adrenals in many cases, and found them profoundly altered; especially was there diminution and disappearance of the lipid substance. In the surgically treated cases subcutaneous injections of  $\frac{1}{2}$  to 1 mg. ( $\frac{1}{30}$  to  $\frac{1}{60}$  grain) of **adrenalin** should be given before or immediately after operation, and repeated on successive days. He believed he had saved some lives by this procedure.

Following the views of Oppel, R. Leriche (C. r. de la Soc. de chirurg. de Lyon, Dec. 10, 1925) performed **unilateral adrenalectomy** in a case of gangrene of the large toe in man of 34 years, due to hyperadrenia, after orthodox measures had failed. The pain was arrested, the ulceration ceased and cicatrization followed. Diez (Prensa Méd., Buenos Aires, Sept. 20, 1925) also obtained excellent results by means of **sympathectomy** in 26 cases of gangrenous trophic lesions of the extremities, such as habitual acrocyanosis, causalgia, mal perforant, etc. No benefit was obtained, however, in 5 cases of gangrene due to obliterating thromboangiitis of syphilitic origin, nor in 1 of acrocyanosis due to arteriosclerosis. S.